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CLINICAL ELECTROCARDIOGRAPHY[1]

DONAL P. MURNAGHAN, M.B., B.CH., F.R.C.P. (C)[2]

AN ELECTROCARDIOGRAM provides information about the electrical activity of the heart muscle, the rhythm of heart action and the state of conducting tissues at the time at which it is recorded. It is of most help in the recognition of arrhythmias and in the identification of localized myocardial damage. It shoulh be fully understood that it has certain limitations: (*a*) it has been frequently stressed that the electrocardiograph should not take the place of a complete history and physical examination; it may add considerable information to the diagnosis and no cardiovascular examination is now considered complete without one; (*b*) it does not offer an etiological diagnosis and does not indicate the prognosis; (*c*) it cannot indicate the presence of valvular disease and certainly does not provide information regarding the state of compensation of a heart or its degree of reserve. Conclusions regarding an etiological relationship are reached only by such correlations as, for instance, auricular fibrillation and evidence of right ventricular hypertrophy which may be found in later stages of chronic rheumatic heart disease with mitral stenosis.

A patient may actually have serious heart disease, for example malignant endocarditis, and have a normal electrocardiogram. The electrocardiogram may be altered by both cardiac and non-cardiac conditions, reversible or irreversible. Temporary conditions may alter the T waves which record, in some way, the repolarization process of the myocardium after passage of the excitatory wave. Knowledge of the numerous reversible or irreversible factors responsible for such a change is obviously important in interpreting the significance of abnormal T waves in any given case. It stands to reason that a physician in possession of all the clinical data on a patient is the best one to interpret an electrocardiogram rather than someone who merely sees the tracing. In lieu of this, however, provision of pertinent clinical data and some information regarding the body build and recent medication of a patient (digitalization especially) give helpful information to the reader of the record. It may be mentioned here that special preparation and care in taking and interpreting the records are essential and of fundamental importance if only to avoid errors which

[1]From the Department of Medicine, The University of Toronto and The Medical Service of the Toronto General Hospital.

[2]Clinical Teacher in Medicine, University of Toronto.

may be interpreted as due to disease in the heart itself.

In an article such as this it is impossible to present in full the application of electrocardiography to clinical medicine. It was thought that the purpose of it might best be served if a routine method of interpretation was presented, normal values discussed, and then, a representative number of illustrations were given and further discussion centered around them. The variety of patterns are numberless and many good atlases with appended clinical information are available for those who wish to go further in this field. The reader should first be familiar with the average normal pattern (Fig. 1).

THE ELECTROCARDIOGRAM

Today, an electrocardiogram consists of recordings of three so-called standard limb leads, I, II, III, and one or more precordial leads. The importance of taking multiple precordial leads has become established during the past ten years. There are six standard positions for locating the exploring chest electrode (after Wilson) but it is not necessary to record all of them in any one patient. The sites are (*1*) fourth intercostal space at the right sternal margin; (*2*) fourth intercostal space at the left margin of the sternum; (*3*) midway between *2* and *4* at the same horizontal level as *2*; (*4*) the fifth intercostal space at the left midclavicular line; (*5*) left anterior axillary line horizontally from *4*; (*6*) left midaxillary line horizontally from *4* to *5*. These are referred to by a numerical subscript to capital letters which refer to the location of the exploring electrode (C) and the indifferent electrode which may be F (for leg), R (for right arm), L (for left arm) or V, the common terminal uniting all three extremities (Wilson). Commonly the precordial leads are referred to as V leads where the central terminal (of Wilson) is used. It is the practice in many clinics to record from only three positions, for example, *1*, *3*, *5* or *2*, *4*, *6*. More extensive exploration than the six positions mentioned may be applicable to certain cases. Three augmented unipolar limb leads can also be used in a study of the electrocardiographic features of any patient. They have special merit in determining the position of the heart as it lies in the chest and in the identification of hypertrophy of one or other ventricle. They are referred to as AV_R, AV_L, AV_F respectively. (The reader is referred to the publications of Dr. Frank Wilson, Dr. E. Goldberger and Dr. G. Myers for further details).

CLINICAL INTERPRETATION

A routine for reading tracings should include observations on rate and rhythm, the PR and QRS durations, any deviation from normal of the QRS complexes, the RS-T segments and T waves. Technical inaccuracies such as incorrect standardization (normally 10 millimetres represents 1 millivolt) and incorrectly applied extremity leads should be kept in mind. Table I gives the variation in normal PR intervals according to Ashman and Hull.

The QRS tracing in precordial leads of a normal heart rises in a positive deflection (the R wave) and is followed by a negative one (the S wave) except over the left ventricle; the R is smallest over the right ventricle and largest over the left; a convenient way to remember this is that the peak of the R wave represents the arrival of the excitation wave at the point under the exploring electrode and the S wave represents the passage of the excitation wave through the remainder of the muscle. When the electrode is over

TABLE I

Upper Limits of the Normal PR Intervals
(Duration in Seconds)

Rate:	Below 70	71-90	91-110	111-130	Above 130
Large Adults	0.21	0.20	0.19	0.18	0.17
Small Adults	0.20	0.19	0.18	0.17	0.16
Children, ages 14-17	0.19	0.18	0.17	0.16	0.15
Children, ages 7-13	0.18	0.17	0.16	0.15	0.14
Children, ages 1½-6	0.17	0.165	0.155	0.145	0.135
Children, ages 0-1½	0.16	0.15	0.145	0.135	0.125

the left ventricle (in the axilla) the remainder of the heart has presumably already received the excitation wave. If the initial deflection in precordial leads is downwards more than three or four millimetres it is suggestive of underlying muscular damage.

ARRHYTHMIAS

Premature Beats

Auricular premature beats occur earlier in the cycle than normal; the P wave is either normal or inverted followed by a QRS similar to that of the normal beats. The length between two beats when interrupted by an auricular premature beat is shorter than two normal cycles. A ventricular premature beat is recognized by its bizarre appearance; the interval between two normal beats which have been interrupted by one is equal to the length of two normal cycles. A compensatory pause follows the ventricular premature beat. If they occur after each normal beat coupling is said to occur; digitalis overdosage may produce such an effect (Fig. 9). Occasional premature beats, auricular or ventricular, are not indicative of heart disease but frequent ventricular ones do suggest its presence.

Auricular Flutter and Fibrillation

Auricular flutter (Fig. 10b) consists of a circus wave in the auricle and presents regular P waves at 280-300 per minute with QRS responses showing variable block, for example, 2:1 or 3:1, etc. The flutter waves are best seen in lead II or with the exploring electrode to the right of the sternum.

Auricular fibrillation shows a wavy baseline with fine fast P wave activity and the striking complete irregularity of the ventricular complexes.

Heart Block

Partial auriculo-ventricular block is present when the PR interval is longer than 0.2 second. This may occur in rheumatic fever, arteriosclerotic heart disease or digitalis therapy. If the PR becomes progressively longer in succeeding beats until complete block occurs, the latter is known as a Wenkebach period.

Complete heart block (Fig. 10d) is recognized by a slow regular ventricular rate of 30-50, with an independent auricular rate of 70-80 per minute. They bear no relationship to the QRS complexes.

Tachycardia

Paroxysmal auricular tachycardia (Fig. 10a) always starts with a premature auricular beat and shows regularly recurring P waves although in some cases not easy to identify, the ventricular rate is usually from 160-200 per minute and regular. In ventricular tachycardia (Fig. 10c) the QRS is usually bizarre, the rate approximately 140-160 per minute with slight irregularities between the complexes when measured with a calipers. The auricular activity is not disturbed but may be impossible to identify. An interesting pattern called the short PR-wide QRS syndrome of Wolff, Parkinson and White is of importance for such a case is prone to short runs of ventricular tachycardia. These are considered benign in contradistinction to those cases of ventricular tachycardia which complicate myocardial infarction.

AXIS DEVIATION

By axis deviation one means that the electrical axis of the QRS complex as calculated on an Einthoven triangle points to a certain direction. Left axis deviation is present when the principal deflection in lead I (R) is upright and the principal deflection in lead III is downwards (S); that is, the principal deflections in leads I and III point away from each other. Right axis deviation is present when they point towards each other. In a transversely placed heart there is left axis deviation while in a vertical heart or hypertrophy of the right ventricle there is right axis shift.

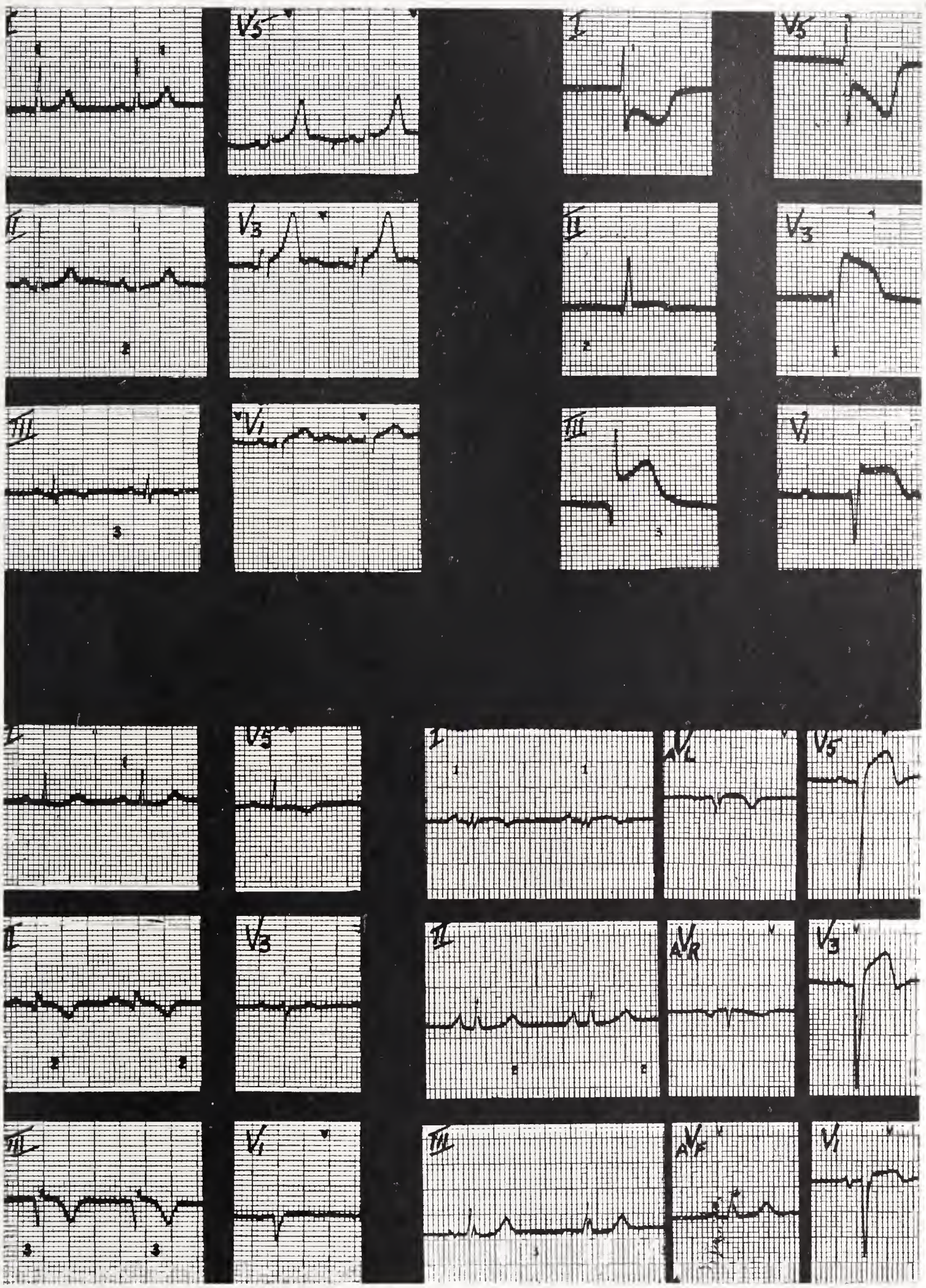
Left ventricular hypertrophy (LVH) produces left axis deviation, with slight depression of RS-T in lead I and negative T in leads I and precordial positions *5* and *6*. Right ventricular hypertrophy (RVH) produces right axis deviation, and a prominent R in the precordial positions *1* and *2*. An S wave persists in the positions *3*, *4*, *5*. Chronic cor pulmonale secondary to pulmonary hypertension is a typical cause of this pattern; in addition the P waves are often large and peaked. In congenital heart disease with right ventricular hypertrophy a similar pattern occurs. Acute cor pulmonale secondary to pulmonary embolism is characterized by an increase in rate, a temporary right axis shift, slight depression of the RS-T in leads *1* and *4*. The S in lead *1* may be widened taking the form of transient right bundle branch block. The transient nature of these changes in serial records confirms the clinical diagnosis.

BUNDLE BRANCH BLOCK

Left bundle branch block (LBBB) and right bundle branch block (RBBB) produce patterns similar to those of left and right ventricular hypertrophy respectively with, in addition, an increase of the QRS to 0.12 second or longer. RBBB (Fig. 6) is associated with a widened S in lead I and a tall late R in precordial positions *1* and *2*. If one recalls the explanation of the normal form of the QRS in precordial leads it will be seen how the late arrival of the excitation wave in the right ventricle produces this characteristic wave form. In LBBB (Fig. 7), T_1 is negative but T in precordial position *5*, *6* are not commonly deeply inverted as in hypertrophy curves.

INFARCTION OF THE MYOCARDIUM

Myocardial infarction, not coronary thrombosis as is often loosely stated, is reflected by changes in an electrocardiogram. The infarction must reach either the endocardial or epicardial surface to



1 2 3 4

FIG. 1—Normal record. In this tracing V_3 and V_5 appear more like V_2 and V_6; heart transverse in a broad chest in this patient. (A deep S is present in V_1 and V_3; a tall R occurs in V_5.)

FIG. 2—Recent posterior myocardial infarction.

FIG. 3—Posterior myocardial infarction, a typical record showing Q_2 and Q_3; negative T_2, T_3 and TV_5.

FIG. 4—Recent antero-septal myocardial infarction. Note the absent R wave in V_3 and V_5. The unipolar limb leads demonstrate a Q and negative T in Lead AVS. In AVS the P wave, QRS complex and T wave appear inverted. This is normal.

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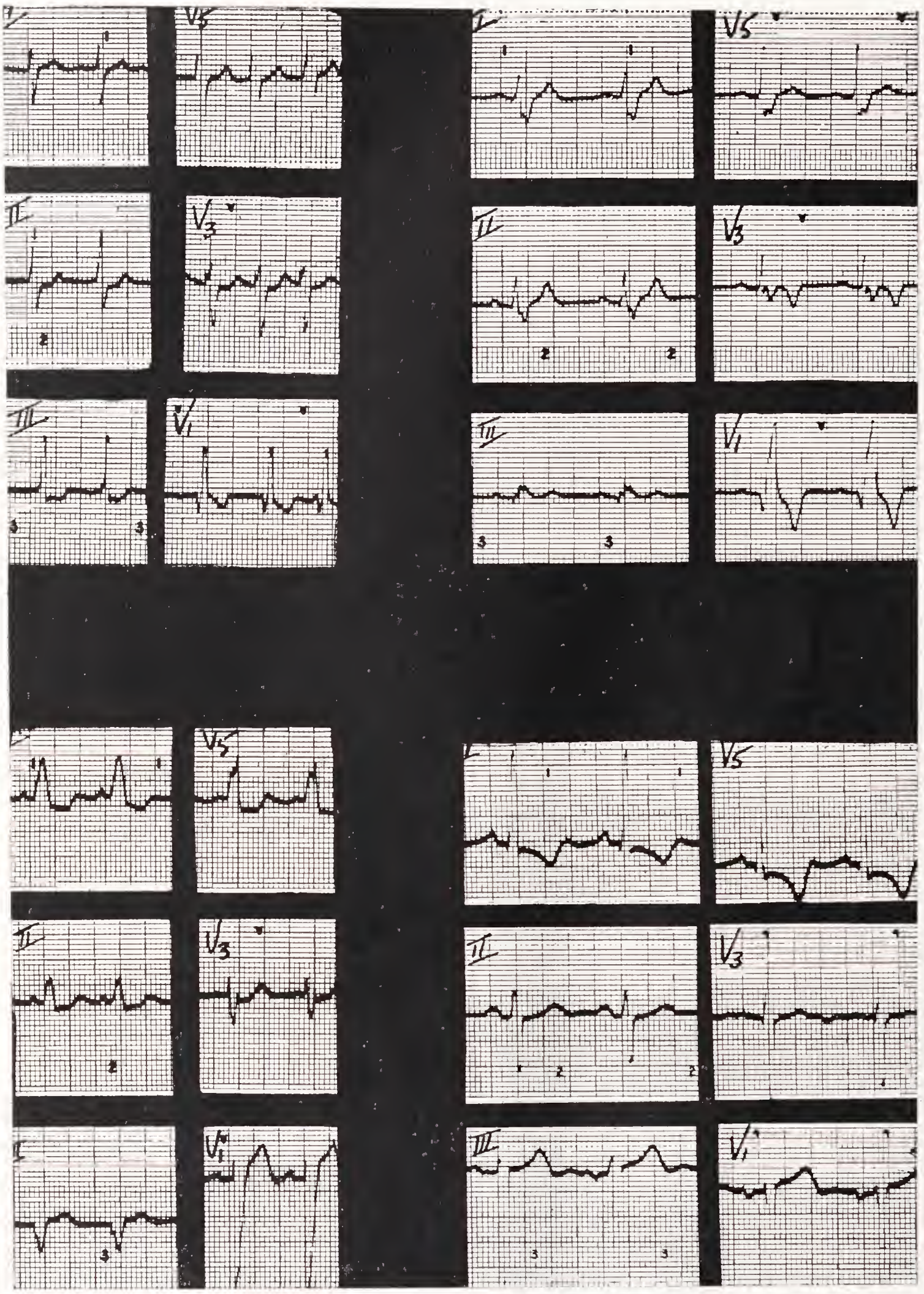

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FIG. 5—ECG of a patient with mitral stenosis; auricular fibrillation (not clearly identified): right axis deviation: Note confirmation of this in a tall $R - V_1$ and deep S in V_5.

FIG. 6—Right bundle branch block: $QRS = 0.16$ sec. Note wide S wave. In V_1 the R wave occurs late and is prominent.

FIG. 7—Left bundle branch block: $QRS = 0.14$ sec.

FIG. 8—ECG from a patient with hypertensive heart disease. Left axis deviation; slight depression of ST_1: Negative T wave in leads 1 and V_5. Typical left ventricular hypertrophy pattern.

alter the electrocardiogram in a diagnostic pattern, that is to produce measurable electrical changes. The area of dead muscle is responsible for the absent R wave in the precordial leads; the adjacent ischemic muscle (injured area) for the RS-T displacement and T wave changes. The latter are always negative over ischemic muscle. Fairly precise localization of the infarction is possible. Only the typical patterns of anteroseptal and basal infarcts are discussed below.

Recent infarction of the anterior surface involving the apex (Fig. 4) shows elevation of the RS-T in lead I, and in precordial positions *3*, *4* and perhaps *5*, with depression of the RS-T in lead III. A Q wave appears in lead I and the initial upright deflection in the precordial positions above noted disappears when the infarct extends through to the epicardial surface. The elevated RS-T segment is a current of injury and is best localized by an exploring electrode over the injured surface. Posterior infarction of the myocardium affects especially the limb leads, II and III; a definite Q wave appears and the RS-T segment is elevated in both leads; the RS-T may be slightly depressed in lead I and precordial positions *5*, *6*; the extent of these changes varies with the size of the infarct (Fig. 3). An electrode in the esophagus behind the heart would be in the best location to identify the injured area.

When the recent change has passed, anterior infarction is associated with a small Q and a negative T in lead I, and absent R (deep initial deflection) in precordial positions *3*, *4*, and *5*, followed by a negative T wave (Fig. 4). The size of the infarct modifies the extent over which abnormal findings are found. In posterior infarction (Fig. 2), a definite Q wave occurs in leads II and III, followed by negative T waves. Pardee gave the name cove-shaped to this particular pattern of a slightly convex ST segment bending over into an angular negative T wave. The T wave in chest positions *5* and *6* may be negative.

There are many atypical patterns in clinical states where myocardial infarction seems a reasonable assumption. Autopsy findings in humans indicate the variability of the extent of infarction, endocardial, intramural or transmural, as well as of the location in the septum, apex, base, or elsewhere. Some cases with extensive degenerative coronary artery disease have diffuse myocardial damage without a specific area of infarction; some demonstrate a changing pattern in serial tracings strongly suggesting infarction where no clinical episode of pain was present. A change in exercise tolerance or the onset of failure may have been the clinical condition of importance. The value of serial tracings, at perhaps 3-7 day intervals, when the clinical history suggests myocardial disease is often overlooked. One record may be normal after a frank pain of coronary thrombosis lasting perhaps one hour because myocardial ischemia has not been present in an area favourable for identification by the particular leads used to study the particular case at that time. Subsequent tracings within from forty-eight to seventy-two hours may indicate the tell-tale site, or may be normal if an area of infarction did not result. This latter is a possibility sometimes overlooked or denied.

The value of literally exploring many areas on the chest near the heart is often neglected for identification of an infarcted site and its approximate size. Such a search, when the usual leads are negative, may be fruitful.

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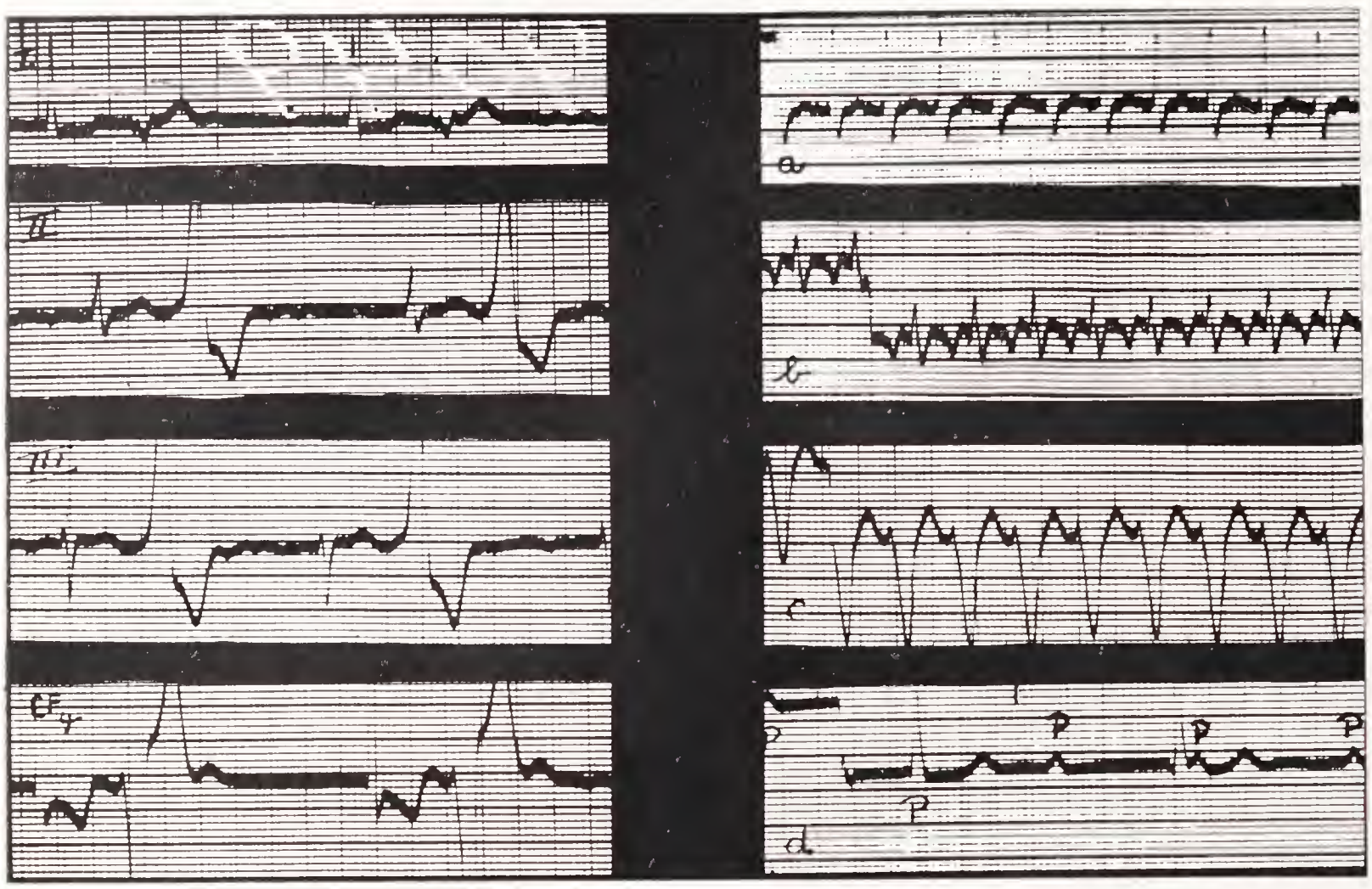

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FIG. 9—Bradycardia: auricular fibrillation: left axis deviation: ventricular premature beats occurring after each normal beat giving bigeminal rhythm. Slight depression of *ST* segments in lead 1 and CF_4. Consistent with digitalis overdosage.

FIG. 10—(*a*) Lead 2: Paroxysmal auricular tachycardia.
(*b*) Lead 2: Paroxysmal auricular flutter with 2 to 1 block; ventricular rate 160 per min.
(*c*) Lead 3: Paroxysmal ventricular tachycardia. Rate 180 per min. Note wide *QRS* complexes.
(*d*) Lead 2: Complete heart block. *P* waves (auricular rate) 75 per minute: Independent ventricular rate (*QRS*) rate 40 per minute.

MISCELLANEOUS EFFECTS

There are miscellaneous non-specific effects on the electrocardiogram which are mentioned only briefly here. Strangely, it is amongst these that some physicians are led astray into etiological relationships with the obvious pitfalls. T wave abnormality, such as inversion in lead I, may result from many causes; it may be reversible and refers only to the order of repolarization. Severe anemia, severe systemic infection, anoxia, hypertensive states, rapid persistent tachycardia, smoking in some persons and drinking of ice cold water (inversion of T_2) are among the many diverse causes of such a change. Digitalis and its derivatives depress the RS-T segments and, often, the following T wave is diphasic in form. Bradycardia or coupling produced by ventricular premature beats also results from this medication.

Abnormalities in electrolyte balance also affect the electrocardiogram. Significant for example are: (*a*) hypocalcemia prolongs the QT interval; (*b*) hyperpotassemia, occurring in diabetic acidosis, is blamed for prolonging and lowering the T waves.

Myxedema and chronic constrictive pericarditis may be associated with normal rhythm, low amplitude of the QRS wave (5 mm.), and iso-electric or low negative T waves in all leads. The ven-

tricular rate may be slow (50-60 per min.) in myxedema. Acute inflammatory pericarditis is associated with an increased heart rate (100-120 per min. perhaps) and an elevation of the RS-T segments in all leads. In this way, it may be distinguished from recent myocardial infarction with its reciprocal RS-T segment displacements in the limb leads, when the clinical features are similar.

There are some electrocardiograms which baffle even the most experienced. It is reasonable to assume in them myocardial damage yet no prognostic value can be attached to the statement unless clinical knowledge of the patient provides the etiology.

SUMMARY

In this short article there are many gaps. Theoretical considerations have been practically omitted. Discussion of the arrhythmias is all too brief. The importance of conservative interpretation of electrocardiograms is inferred throughout; serial tracings at intervals of 3-7 days are often helpful in the elucidation of suspected myocardial ischemic damage. Daily records are rarely necessary; when attempts are being made to convert an arrhythmia to normal sinus rhythm they may be of help. The value of using multiple precordial positions is now established and should be part of routine electrocardiography, more especially where disease is present or suspected.

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HEADACHE

GEORGE A. TRUSLER, 4T9

HEADACHE, a very common complaint, is also a very important symptom. Not only does it aid in the diagnosis of a patient's disease, but it also gives valuable information as to the kind of a person the patient is. From this knowledge the physician is able to assess the proportions of functional and organic disorders causing the patient's symptoms.

In this paper, the term headache is taken to include any pain in the head and an attempt is made to describe the different types of headaches, their characteristics and how they are produced. For the sake of simplicity, the most widely accepted etiological theory for each type is stressed and certain others merely noted. It must not be thought that these theories are definitely established. In some cases, the treatment is mentioned.

ANATOMY AND PHYSIOLOGY

Using a variety of stimuli during surgical procedures on the head, Wolff and his co-workers came to the following conclusions regarding pain sensitive structures:

"1. Of the tissues covering the cranium, all are more or less sensitive to pain, the arteries being especially so.

2. Of the intracranial structures, the great venous sinuses and their venous tributaries from the surface of the brain, parts of the dura at the base, the dural arteries and the cerebral arteries at the base of the brain, the fifth, ninth and tenth cranial nerves, and the upper three cervical nerves are sensitive to pain.

3. The cranium (including the diploic and emissary veins), the parenchyma of the brain, most of the dura, most of the pia-arachnoid, the ependymal lining of the ventricles and the choroid plexuses are not sensitive to pain."

The sensory division of the trigeminal nerve supplies the superior surface of the tentorium cerebelli and all the pain sensitive structures above it. Pain in this area is felt in front of a line drawn vertically from the ears across the top of the head.

Pain felt behind this line is carried chiefly by the ninth and tenth cranial nerves and the upper three cervical nerves from pain sensitive structures on or below the inferior surface of the tentorium cerebelli.

In addition, Wolff *et al.* postulate six basic mechanisms of headache from intracranial sources:

"(*a*) traction on the veins that pass to the venous sinuses from the surface of the brain and displacement of the great venous sinuses; (*b*) traction on the middle meningeal arteries; (*c*) traction on the large arteries at the base of the brain and their main branches; (*d*) distension and dilation of intracranial arteries; (*e*) inflammation in or about any of the pain sensitive structures of the head, and (*f*) direct pressure by tumors on the cranial and cervical nerves containing many pain afferent fibres from the head."

In brief, therefore, cranial vascular structures are thought to be the commonest source of pain. The principle mechanisms are inflammation, traction, displacement and distension.

HEADACHES DUE TO INTRACRANIAL LESIONS, SPINAL PUNCTURE AND VENTRICULOGRAPHY

Intracranial tumors cause headache locally, by traction on pain-sensitive structures, and at a distance, by displacement of the brain. Increased intracranial pressure in itself is not responsible. For this reason, the headache overlies the tumor in only one-third of

the cases or in two-thirds of them if there is no papilledema. With posterior fossa tumors, headache, usually the first symptom, is almost always over the back of the head; whereas with supratentorial tumors, headache is the first symptom in only about one-third of cases and is usually more anterior.

The pain varies from a sharp severe stabbing to a deep dull ache. It may be continuous or intermittent. Sudden postural changes, stooping, straining, and jolting aggravate the headache, and it is often worse at night or in the early morning. Usually not so severe as migraine, it rarely interferes with sleep and may often be relieved by acetylsalicylic acid or cold packs. If present, nausea is slight unless the pain is severe. Vomiting, sometimes projectile, may occur due to displacement or compression of the medulla, but without relief of the headache.

Post-traumatic headache is commonly of psychogenic origin. Occasionally it may arise from actual brain damage with resulting scar formation. Otherwise, the pain is thought to be due to an increased awareness of normal head sensations with or without sustained contractions of head and neck muscles. The headache is intermittent and often localized close to the site of the injury. Postural changes, effort, fatigue or emotional upsets may precipitate it. Stooping, straining, looking upward and changes in weather may aggravate the headache. Treatment consists of early ambulation, speedy compensation and reassurance.

Penfield postulated that adhesions of the arachnoid mater to the dura mater were formed while the brain was in an abnormal position in the skull as a result of cerebral edema. On disappearance of the edema the brain would shift back to its normal position with resulting traction of the adhesions on pain-sensitive structures. To break these adhesions, Penfield advises the removal of fluid and injection of air into the subdural space.

Lumbar puncture, spinal anesthesia, encephalography and **ventriculography** may produce headache secondary to a prolonged leakage of fluid through the dural hole produced by the operator's needle. Wolff *et al.* were able to induce headache in erect humans by withdrawing 20 cc. of cerebrospinal fluid, thus increasing the negative pressure at the vertex from 150 to 220 mm. of water or higher. Restoration of the cerebrospinal fluid volume gave relief. As in the case of lumbar puncture, the headache was relieved by simple flexion or extension of the head or by lying down. Consequently, the headache is explained as being due to increased traction on the veins anchoring the brain to the roof of the skull plus a venous vasodilatation due to the lessening of support given the veins by the cerebrospinal fluid.

The method of preventing the headache following lumbar puncture varies, some observers advocate one or two days bed rest; whereas others feel that the patient should avoid any period of recumbency. Two or three hours rest, however, would seem advisable.

Meningitis usually produces an occipital or generalized headache, excruciating, throbbing and aggravated by bending, stooping, lifting and straining. The headache of more **chronic infections** such as syphilis is less severe, slow in onset and tends to be nocturnal. **Brain abscess** and **aneurysm** produce head pain similar to that of a tumor. **Subarachnoid hemorrhage** gives a headache which is often sudden, severe

and suboccipital, whereas that associated with **chronic subdural hematoma** is less severe, dull and occurs weeks or months after the injury.

Cerebral arteriosclerosis is accompanied by a dull, heavy bregmatic pain which occasionally may be sharp, stabbing and localized. It is believed due to either distension of weak arteries or traction on pain-sensitive sites from cortical atrophy from obliterating disease of the small cortical blood vessels.

CRANIAL NERVE NEURALGIAS

These neuralgias characteristically produce headaches which are unilateral, severe, sharp, lancinating, paroxysmal and follow the distribution of the nerves involved. In some cases, neoplastic or inflammatory disease near the involved nerve is responsible. In other cases the etiology is undetermined.

Trigeminal neuralgia (**tic douloureux**), the commonest form, is most often seen on the right side and along the distribution of the maxillary branch of the fifth nerve. It affects the sexes equally and chiefly about the fifth decade. The pain is unilateral, sudden and severe, lasting seconds to minutes and recurring repeatedly at irregular intervals. As time goes on the intervals become progressively shorter and the pain more severe. Pressure on tender, hypersensitive "trigger zones" along the course of the nerve may incite the pain, as may also such acts as washing the face or brushing the teeth. Frequently trophic and secretory changes such as moist flushed skin, eruptions, conjunctivitis and salivation are present in the area involved. Lewy and Grant consider that in many cases trigeminal neuralgia is a special form of the thalamic syndrome caused by functional or organic vascular insufficiency and occurring in a group of persons of similar hereditary and constitutional physical habitus and mental make-up with a tendency to cardiorenal angiopathies. Treatment consists of alcohol nerve block and if this fails, division of the posterior sensory root of the Gasserian ganglion.

In **sphenopalatine neuralgia,** the pain occurs about the eye, the upper jaw and the teeth extending backward under the zygoma to the ear with resulting earache and pain in the mastoid. If severe, it may extend to the occiput, neck, shoulder or even down the arm to the hand. It may be constant with exacerbations, alternately on and off, cyclical as migraine or stabbing and sharp as a tic. Occasionally, there is associated sneezing, rhinorrhea, lacrimation, photophobia, vertigo and slightly diminished sense of taste on the anterior half of the tongue. Specific treatment consists of cocainization or alcohol injection of the sphenopalatine ganglion.

Glossopharyngeal neuralgia is characterized by a unilateral, excruciating, usually paroxysmal pain of a few seconds duration. Irritation of the "trigger zone" located in the tonsillar region or back of the tongue while eating, swallowing, chewing or speaking may incite the pain which radiates to the ear and down the throat. It may be associated with burning and dryness of the throat. Cocainization of the throat will often relieve this pain. In some cases, intracranial section of the ninth nerve is advised.

Neuralgia of the nervus intermedius is an uncommon condition associated with severe paroxysmal pain in front of the ear and over the mastoid process. Cocainization, alcohol block and section of the nerve are suggested treatments.

Tympanic plexus neuralgia (**Jacobson's tic**) is also an uncommon cause of head pain. It is distinguished by paroxysms of severe, stabbing pain deep in the external auditory canal. Ninth nerve section gives complete relief.

Mandibular joint neuralgia (**Costen's syndrome**) refers to neuralgias and ear symptoms associated with disturbed function of the temporo-mandibular joint. It usually occurs in a partially or completely edentulous mouth, with changes in the joint due to the over-closure of the jaw. The pain may be a headache about the vertex and occiput and behind the ears or a burning or dry sensation in the throat, tongue and side of the nose. Ear symptoms are tinnitus, dizziness and dull pain or merely a stuffy sensation. These are most marked at mealtime. Correction of the overclosure with a suitable denture will give permanent relief.

HEADACHE OF OCULAR ORIGIN

Ocular headache has been defined by Weeks as "that acute discomfort in and about the head that directly or indirectly comes from organic or functional disorders of the visual apparatus." It is a relatively common cause of headache though not so common as popular opinion would indicate. The pain may arise from direct local stimulation of some pain-sensitive ocular structure, from reflex myalgia or from occipital myalgia which is due to the strain of holding the head in a certain position to avoid further strains of changing accommodation. In general, ocular headaches are characteristically dull, of slow onset and gradually become more severe and localized. They are aggravated by light, reading, noise and travel. The photophobia is thought to be due to a combination of the light reflex and ophthalmic irritation.

Conjunctivitis and **corneal abrasions** or **ulcers** manifest chiefly a local itching or burning. In **dacryocystitis,** the lacrimal ducts and orbit are the seats of the pain. **Iritis** gives pain referred to the orbit, temples and side of the nose. In **choroiditis** and **retinitis**, the pain is over the brow and often radiates to the back of the head. **Retrobulbar neuritis** is associated with vertical, frontal and orbital pain aggravated by pressure and motion.

In **acute glaucoma**, the pain is deep in the orbit and radiates along the branches of the trigeminal nerve with pressure pain in the temporo-frontal region. Sometimes severe enough to cause nausea and vomiting, it is usually worse at night. The pain is due to increased intraocular pressure.

Hyperopia is associated with a frontal or occipital headache usually in the afternoon. It is caused by fatigue and spasm of the ciliary and external ocular muscles owing to excessive accommodation and convergence. **Myopia** rarely results in headache unless it is severe, progressive or unequal in the two eyes. In **astigmatism**, the headache is similar in type and mechanism. The continual altering of accommodation in an effort clearly to focus the eyes causes ciliary muscle fatigue and spasm.

Muscular imbalance seen as heterophoria or strabismus is the commonest ocular cause of headache. Often delayed, appearing in the afternoon or evening and perhaps associated with nausea, nervousness, irritability or a feeling of exhaustion, the pain is commonly referred from deep in the orbit to the occiput and neck. It is due to sustained contraction of the extraocular muscles and the muscles of the scalp and neck.

Panorama headaches are uncommon and occur in people during or after

travelling, without any detectable abnormality in the function of the eyes being present. They are acute and of variable location. Being due to continual accommodation and convergence while watching the landscape, these headaches are successfully treated by having the traveller ride backwards, watch only distant objects or cover the eyes.

Another rare cause of headache is **anisoiconia** in which condition there is a difference in the size and shape of the ocular images in the two eyes as interpreted by the cerebral cortex. The headache is variable and associated with use of the eyes. Diagnosed by a special apparatus, this cortical disorder may be treated by applying the proper lenses.

HEADACHE OF NASAL ORIGIN

Contrary to popular opinion, this is not a common cause of headache.

Experimentally, Wolff *et al.* have found that the mucosa covering the approaches to the paranasal sinuses is the most pain-sensitive and the mucosa lining the sinuses is of relatively low sensitivity. Most of the pain arises from inflammation and engorgement of turbinates, ostia, naso-frontal ducts and superior nasal spaces and it is referred to regions of the head supplied by the second, and to a less extent the first, division of the fifth cranial nerve. Procedures increasing venous pressure and states increasing engorgement of the mucosa such as: anxiety, resentment, cold air, menstruation, sexual excitement and alcohol intensify the headache. Shrinkage by ephedrine diminishes the intensity of the headache. Some authorities believe that many headaches result from the formation of a vacuum in the sinuses by the absorption of air following blockage of the ostia. However, in view of the low sensitivity of the mucosa lining the sinuses, this theory is not generally accepted.

In **acute sinusitis**, the pain is sharply localized, constant or periodic, and starts on arising or shortly after. It subsides in the afternoon, leaving a feeling of pressure or fullness.

In **acute maxillary sinusitis**, the pain is over the frontal area, cheek, upper jaw and teeth, with local tenderness over the sinus and acute tenderness of the upper teeth on chewing.

Headache is the most constant and prominent symptom in **acute frontal sinusitis**. It occurs over the sinus and along the supra-orbital nerve occasionally involving the entire half of the head. Sometimes throbbing and accompanied by nausea, it may simulate meningitis.

The **ethmoid sinuses** are the most commonly affected sinuses. From the anterior ethmoids, the pain is referred to the root of the nose above the inner angle of the eye. The posterior ethmoids refer pain to the temples, to the front teeth and, occasionally, to parietal and suboccipital regions. Burning of the eyes and lacrimation may occur.

In **acute sphenoid sinusitis**, the pain is inconstant and deep. It may be felt behind the eyeballs, over the vertex, in the posterior half of the head or just behind the mastoid process. Commonly there is associated dizziness on stooping.

Chronic sinus disease is associated with a more inconstant diffuse indefinite pain. It is aggravated by jarring, stooping, severe mental or physical effort and loss of sleep.

HEADACHE OF DENTAL ORIGIN

Sensation in the teeth is subserved by branches of the maxillary and mandibular nerves. Locally, a burning, aching sensation is felt, which, if severe, is

accompanied by a steady aching with superficial hyperalgesia and tenderness along the course of the affected nerves. Later, occipital headache may occur due to contraction of neck muscles. If severe and prolonged, pain may be referred along the branches of the ophthalmic nerve as well.

HEADACHE OF AURAL ORIGIN

Lesions in the ear, in addition to local pain, may refer pain along any aural sensory branches from the trigeminal, facial, glosso-pharyngeal and vagus nerves. Reflex disturbance and spasm of auricular, masseter, temporal and occipital muscles result in pain and tenderness. Conversely, lesions affecting any of the aforementioned nerves may refer pain to the ear.

HEADACHE ORIGINATING IN THE NECK

Hypertonia of the neck muscles is a very common cause of headache. The pain is usually suboccipital and may radiate up to the occiput and down between the shoulders. Although it varies widely in severity, it rarely awakens the patient. It is eased by resting the chin in hands. Anorexia, nausea, vomiting and vertigo are sometimes associated with the headache. This condition may arise secondary to other conditions such as: sustained contraction of external ocular muscles, pansinusitis, migraine and emotional tension. On the other hand, it often arises spontaneously for no known cause. With painful nodules present on palpation the diagnosis of fibrositis is applied.

Arthritis of the cervical spine sometimes causes a pain which begins in the occiput but as it becomes more severe tends to spread upward and forward into the temporal region and down into the neck. It gradually progresses to become constant. Most severe in the morning, it often awakens the patient. Aggravated by flexion or extension of the head and by draughts and work, it would seem that tension of the neck muscles is a factor. The pain is usually due to either nerve root compression by narrowing of intervertebral foramena, associated myofibrositis or, rarely, herniation of a nucleus pulposus.

Atlanto-occipital lesions may cause pain in the suboccipital region radiating down the neck to the shoulders. Intermittent or continuous, it may be associated with dizziness and a sensation of grinding on turning the head. The pain is believed due to radiculitis or muscle spasm which results from such lesions as asymmetry or displacement of occipital condyles, congenital fusion of one or both condyles, arthritic changes, asymmetry of the lateral masses and irregularity, fracture, tilting or dislocation of odontoid processes.

HEADACHE DUE TO SYSTEMIC DISORDERS

Essential hypertension may be associated with a severe throbbing headache which awakens the patient or appears on waking. It is most intense before rising and diminishes during the morning. It may be generalized or first affect one area of the head. Available evidence indicates that this headache is due to the increased amplitude of pulsations in the cranial arteries, chiefly extracranial, and that the intensity of the pain is related to the contractile state of the vessels rather than to the degree of hypertension. As in migraine, its occurrence is related often to emotional stresses and adverse life situations.

The headache of **hypertensive encephalopathy** is intense, localized, of

definite onset and culmination and probably due to cerebral edema with traction on or displacement of the tributary veins of the great venous sinuses.

Arteriosclerosis in itself seldom causes headache unless it is accompanied by hypertension.

In **glomerulonephritis** and **uremia** the headache is due to the associated hypertension, uremic meningeal irritation or edema of the brain.

High fever often causes a headache due to increased amplitude of pulsation of cranial arteries. Relief by increasing the intracranial pressure would indicate that chiefly intracranial arteries are affected. At first, the pain is throbbing but, gradually, it increases to a constant severe pain accentuated by each heart beat. Usually bitemporal and frontal, the pain may also be felt in the occiput and down into the neck. In many cases, eyeache is also present and is thought to be due to an orbital vascular disturbance.

Headache associated with constipation, chronic fatigue and indigestion is probably due to the emotional tension causing those complaints.

Temporal arteritis, a condition of the temporal artery pathologically similar to periarteritis nodosa in other arteries, starts with severe temporal pain, leukocytosis, fever and sweating. From two to six weeks later, the area over the affected segment of the temporal artery becomes red, prominent and pulseless. Recovery occurs in several months with no disability unless there was an associated retinal arteritis, in which case there may be failing vision.

Headaches due to **hypoglycemia** and **caffeine withdrawal** are slow in onset and are thought to be due to dilatation of intracranial arteries.

Headaches are frequent in early **syphilis**, occurring during the secondary stage or during mucocutaneous relapses. Of variable severity, they are dull, diffuse, intermittent, occurring daily or semiweekly for months. There may be associated dizziness, nausea, vomiting, insomnia and psychic disturbances. In late syphilis, headaches indicate involvement of the central nervous system.

HISTAMINE HEADACHES

In 1939, Horton described an excruciating, constant, boring, burning hemicranial pain confined to the distribution of the external carotid artery. Found chiefly in the later age groups, this headache will often awaken the patient one or two hours after falling asleep and will last from fifteen minutes to several hours. Associated with it are profuse lacrymation and congestion of the eye, rhinorrhea, increased surface temperature and swelling of the temporal vessels on the same side of the face. At the time, Horton suggested the term erythromelalgia of the head but this has since been changed to histamine headache.

These headaches are eased by assuming the erect posture, compressing the carotid artery or administering ephedrine or epinephrine. Experimental injection of histamine will reproduce the headache in these people. However, injection of histamine will also reproduce the headache of brain tumors or migraine. After this injection there is, at first, a prompt fall in blood pressure which is followed shortly by a slow compensatory rise above the resting level. Schumacher and Wolff indicate that the pain is due to an increased amplitude of pulsation of the large vessels at the base of the brain, especially those of the circle of Willis.

That this syndrome is an actual clin-

ical entity has not met with complete agreement. Gardner *et al.* call it neuralgia of the greater superficial petrosal nerve whereas Kieney believes it is merely an expression of migraine. Treatment is histamine desensitization or the use of the antihistaminic drugs.

MIGRAINE

Migraine is a variable symptom complex with four classic components: hemicranial headache, gastrointestinal disturbances, visual disturbances and familial tendency. Any one of these may predominate and one or more may be absent. It is more common in women, city dwellers and mental workers, and the first attack usually occurs between the ages of sixteen and thirty-five years.

The etiology of migraine is still in dispute. The best theory would seem to be that of Wolff who suggests that the pain is due to an increased amplitude of pulsation in the cranial arteries, chiefly branches of the external carotid artery. Of these, the temporal artery is affected most, thus accounting for the relief often felt by compression of this vessel. An initial cerebral vasoconstriction accounts for the prodromal symptoms. If the increased pulsation of the cranial arteries continues for several hours, the vessel walls become thickened and rigid with edema. With the resulting diminution in pulsations, the pulsating pain is replaced by a steady ache and the artery becomes tender to palpation. For this reason, vasoconstricting drugs are most effective when administered early. After the headache has gone on for some time, there is a painful, reflexly sustained contraction of the muscles of the head and neck. This may last after the primary cause has disappeared.

However, the cause of this vascular disturbance is unknown. It is acknowledged that heredity plays a leading role. Rowbotham postulates that the migrainous individual is born with an unstable hypothalamic mechanism which reacts to the many stimuli reaching it and sends impulses along the motor side of the autonomic pathway to the vessels concerned.

Many migraine sufferers possess similar personalities. They are often ambitious, meticulous, exacting, hard-driving individuals who are sensitive to criticism. The migraine attacks start when the individual has to take responsibilities and be mature and may be responses to stress by an unstable rigid personality. In these patients, emotional conflict will precipitate an attack. Also, some observers find a high incidence of migraine in hypertensive and epileptic persons and vice versa.

Among the other theories as to the etiology of migraine, that concerning a possible allergic origin is much favoured. The high incidence of eosinophilia and other allergic phenomena lends support to this theory.

Endocrine changes are also regarded as potential etiological factors. The frequent association of migraine attacks with menstruation and their absence during pregnancy, with postpartum amenorrhea and after the menopause favour this attitude.

The symptoms of a migraine attack are usually stereotyped for the individual but vary from person to person. Headache is usually the most prominent symptom, being often incapacitating and associated with the wholehearted desire of the individual to be left alone. It starts as a throbbing over either small patches or the whole side of the head. It may shift during an attack and, toward the end as it becomes more steady,

it becomes diffuse over the head and/or extends into the face, neck, shoulders or arms.

Prodromal symptoms or aura may be present or absent. These occur hours to days before the attack and may be of almost any type. Some common ones are visual scotomata, malaise, fatigue, euphoria, belching and diarrhea.

Associated symptoms are those occurring with the headache. Again, these may be of any type, the commonest being visual or abdominal. From these symptoms, various types of migraine are sometimes differentiated. Although many cases bridge these categories, they do suggest the different forms in which migraine may be seen. Common migraine refers to the attack with only headache as a symptom. Ophthalmic migraine refers to the case where the headache is preceded, accompanied by or succeeded by visual sensations such as scotomata or fortification figures. What was once called ophthalmoplegic migraine, occurring with paralysis of the eye muscles lasting two to ten days, is now thought to be usually due to an aneurysm of the circle of Willis. Facioplegic migraine is an uncommon type associated with Bell's palsy. Abdominal migraine is relatively common and may occur with or without headache. The symptoms may simulate any condition of the internal organs, nausea and vomiting or "biliousness" being very common. Psychic migraine is described in which psychic equivalents may obscure or replace the headache, resulting in transitory confusion, depression, compulsions, amnesia or dual personality. In children, migraine is sometimes represented by peculiar attacks of fatigue, depression and irritability with nausea and vomiting and anorexia. The headache may not start until puberty.

The migraine attack terminates gradually after lasting anywhere from fifteen minutes to ten days. The average duration is about twelve hours. There are rarely any sequelae following an attack.

Treatment is divided into general and specific measures. The patient should be instructed regarding a healthy way of life. Overwork and fatigue should be avoided, and adequate rest and relaxation should be obtained each day. Emotional conflicts will very often be found to precipitate attacks. It is the doctor's duty to discover these and to show the patient not only how they act but how they may be avoided. Female patients can be told that they will receive at least partial relief shortly after they reach the menopause.

Specific treatment is principally in the form of drug administration. In a few cases with slight headache, aspirin or codeine may give adequate relief. Potassium thiocyanate, prostigmine bromide, methyl-iso-octenylamine, trichlorethylene inhalation and oxygen inhalation have all been tried with some good results. However, ergot preparations are as yet the most widely acclaimed. They act by causing constrcition of the dilated cranial vessels. Care must be taken in their administration because of this high vasoconstrictive action. Their use is contraindicated in obliterative vascular disease, septic states, hepatic or renal disease and Vitamin C deficiency. Ergotamine tartrate is the most favoured drug and, if used properly, is effective in many cases. It may be given intramuscularly in doses of 0.25—0.5 mg. but no more than 0.5 mg. should be given in one week. Orally, it is given in 3.0 mg. doses with a limit of 10.0 mg. per week, but is not so effective and often is nauseating. For best results, the drug should be admin-

istered as soon as the patient realizes an attack is about to start. Ergonovine and dihydroergotamine are less toxic ergot preparations. Tablets combining ergotamine tartrate, belladonna and phenobarbitone are available for oral use, and seem to have a satisfactory effect with less nausea.

In patients subject to attacks of very severe and incapacitating migraine, Rowbotham suggests cutting the autonomic motor pathways to the vessels. His operation consists of removing the lower half of the superior cervical ganglion, stripping the internal and external carotid arteries of nerves and dividing the external carotid arteries. In his small series of cases, he has had good results with this drastic treatment.

HEADACHE OF EMOTIONAL ORIGIN

Psychogenic headache, the most common type, occurs as a response to stress. It may be the response of an inadequate personality to ordinary stress or the response of an adequate personality to extraordinary stress.

The type of headache often aids in diagnosis. It is usually a sense of constriction or pressure occurring over a poorly localized area. Variable in location, duration and severity, the headache has often been present for years. Worry, fatigue and excitement will initiate it. Although this knowledge is helpful, the diagnosis is essentially based upon the two factors: personality and stress. The doctor's first duty is to know his patient. Only by talking to him and finding out what he likes and dislikes and how he reacts in different situations can this be done. The ultimate object is for the doctor to be able to imagine himself in the patient's position and view life through the patient's eyes, as it were. Only in this way will a satisfactory diagnosis be made and satisfactory treatment be effected. When this is done, the next step is to determine what stress is causing the patient to react with a headache. Only by a complete and often lengthy review of his personal and family histories is this possible.

Given a personality reacting to some stress with the production of headache, the difficulty is to decide what causes the sensory stimulus perceived as pain in the head. In many cases this seems to be due to painful sustained contractions of the muscles of the head and neck. An exaggerated awareness of normal sensations arising in the head has been suggested as another cause. However, in truth the origin of the pain sensation in many cases cannot be explained.

Treatment demands time and patience on the part of the physician. A good rapport must be established and complete examination done to reassure the patient. Knowing the patient, the cause of the headache is explained fully in a manner which the patient will understand. Similarly, a way to correct the aggravating situation is suggested. If the problem is serious, more extensive psychotherapy such as altering the unwholesome environment or removing the patient from the environment is indicated.

However, the commonest headache is one which the doctor is rarely called upon to treat, for it is regarded as a part of our everyday life. It is the dull, generalized, oppressing headache associated with a decreased sense of well-being, which occurs when we are fatigued or worried. Mild analgesics or rest will usually give relief. It is classed with

headache of emotional origin because of its similar mechanism of production. However, because it occurs in normal healthy people who cannot be classed as psychoneurotic, it must be distinguished from important psychogenic headaches.

INCIDENCE IN GENERAL PRACTICE

In conclusion, it might be well to indicate the frequency of occurrence of these different types of headaches as they might appear to a doctor in general practice.

Where headache is the presenting symptom, psychoneurosis is the commonest cause. Next, in order of frequency are migraine, lesions of the eye and nose and lastly chronic infections and intoxications. In these cases, the physician must beware of unconsciously accepting the diagnosis which the patient will often suggest.

Where headache is but one of a group of symptoms, psychoneurosis is again the commonest cause, with fever and septicemia ranking second. Lesions of the eye, nose and ear, intracranial lesions and systemic conditions such as hypertension or chronic nephritis account for most of the remaining cases.

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PREMEDICAL STUDIES

II. CHEMISTRY AND MEDICINE[1]

L. JOSLYN ROGERS, B.A. Sc., M.A.[2]

CHEMISTRY is considered one of the basic sciences necessary in any medical course. The reason is readily apparent if one reviews the history of certain developments over the past years.

The earlier anesthetics were the products of the chemical laboratory. There, the substances were produced and the quality was rigidly controlled by exacting analytical procedures. The modern anesthetics and sedatives, which have been such a boon to both the medical profession and the patient, have followed the same pattern.

In the field of sanitation, where water and sewage treatment are vital factors in public health, chemistry plays a leading role. The control of communicable diseases, which can be spread by the common use of culinary articles, particularly cups and glasses, is effected by chemical means—the use of hypochlorites, now a matter of law in Ontario. The medical officer of health should know what these compounds are, the standards under which they are sold and how to use them effectively.

In recent years, it has become the custom among many of the larger industrial firms, to employ a doctor either on a full-time basis or as a regular consultant. While the general health of all workmen is of great importance to the employer, he feels that his first responsibility is to take every precaution available to him to protect his staff of men from occupational hazards. Many of these arise from materials being handled by workmen—some being universally toxic, but many causing great discomfort and distress due to the particular individual's sensitization. Because Canada is now a highly industrialized country with almost every type of chemical employed in production of manufactured goods, the physician is faced with the need of understanding this phase from a most basic standpoint.

We have in Ontario an excellent example of a direct contact of chemistry and medicine. In our mines, the men are exposed to the silica dust from rock which causes the disease known as silicosis. Due to intensive research work, it was found that by treating the workmen with aluminum powder much of the ill effect of the rock dust was overcome. This relief was obtained by the combined efforts of the doctor and the chemist.

No apology is required for chemistry, or any other basic science, in the practice of medicine. He who administers a medicine knowing what will be effected and why, will have success and, in all probability, during his career, in some way, he will improve medical practice. He who administers medication because it is advertised, popular, or fashionable, is proceeding without real knowledge and will have doubtful results.

The human body is a delicate chemical

[1]Part I was *The Place of Physics In Medical Training*, by R. W. McKay, THIS JOURNAL **26**, 140 (1949).

[2]Professor of Analytical Chemistry, University of Toronto.

laboratory where sensitive controls are maintained by elaborate chemical systems, all following fundamental chemical principles. The greater the understanding we have of such principles, the better we shall know how to assist the body under the storm of disease. Look to the fundamentals to obtain the ultimate, desired result.

The long and close association of medicine and chemistry might be inferred from the following translation of Horace by Kipling;

> "There are those, whose study is of smells,
> And to attentive schools rehearse
> How something mixed with something else
> Makes something worse.
>
> "Some cultivate in broths impure
> The clients of our body—these,
> Increasing without Venus, cure,
> Or cause disease."

III. PREMEDICAL ENGLISH

MILLAR MacLURE, M.A.*

THE PREMEDICAL STUDENT in this institution is in an ambiguous position. He commands respect not only by his own talents but by the prestige of the faculty to which he has secured conditional admission. At the same time, he has still to prove himself, and, as he moves about from one building to another, he must feel like an instructor in English reading one of the elaborate introductions which often raise the curtain on a freshman essay: when do we begin?

Let him comfort himself by reflecting that he began long ago, and that a year finished ends nothing but only begins something new. If a doctor stops being a student he is only a quack. If a premedical student thinks in terms of accomplishment and not in terms of things still to be accomplished he may not even get a chance to be a quack. This education is a serious affair, not to be undertaken lightly, with your fees paid and your girl friend in the same town, but discreetly, soberly, and in the fear of God. I consider it is our business as instructors in English to premedical students to instil some of this discretion, sobriety and perhaps even a little of the fear of God.

Perhaps one main value of a course in English for would-be professionals (who have the attitude of professionals even before they are really so) is that it teaches accuracy. This may seem superfluous for persons whose training involves a rigid discipline of laboratory experiment, but such a discipline usually leaves the student woefully sloppy in everything else but a few special techniques. The proceedings of professional societies when they come to examine the phenomena of living in general instead of the behaviour of certain bacteria or certain radioactive materials are frightful examples of this fuzziness which the study of the art of expression seeks to correct. I distrust a man who leaves out apostrophes (unless he is Bernard Shaw) just as much as I distrust a man who leaves a sponge in the incision. Both are poor citizens and enemies of humanity. To write accurately is every

*Lecturer in English, University College, University of Toronto.

bit as much a mark of civilization as the ingenious removal of a diseased organ or the development of a germ-killing product from a mold. In the words of Sir Ralph Bloomfield Bonington, one must stimulate the phagocytes, and anything will do, a well-tied suture or a well-turned sentence. Generations of ill-chosen teachers of English have nourished the impression that any old thing, any high-sounding imbecility, will do for study in the humanities. Vague stuff, the scientists call it. But when you are ill you must have the best doctor, the dose must be measured most accurately, nobody must make any mistakes, or you might die. The death of the mind, the slow putrefaction among mental phantasms, the crucifixion of the intellect upon diverse and meaningless slogans, is only lately recognized once more by either students of the humanities or students of medicine as a sickness more terrible than any physiological disorder. Learn to think and learn to think by learning to express your thoughts and you save your body, and perhaps your soul too. Those old fogies in the middle ages were not such fools when they suggested you save your soul first.

Now in the matter of knowledge, which is sobriety, there is much the student may learn from the study of literature, any literature, but specifically from the literature of his own national tradition. He will learn that there is no single answer, no ingenious formula, to explain all things. So long as he has not seen this simple truth, he will continue to attend lectures on, say, *Hamlet*, his notebook clutched in his hot little hand, ready to take down the magic words, the charm, the incantatory phrase which will open that dark text for him for ever. When he does apprehend this little axiom, which is negative only in seeming, he will have learned that human affairs proceed by paradoxes and ambiguities, that the precipitate in the human equation is not of one colour, that just because there is no answer, no little amulet to wear around your neck like a witch-doctor or a lover, life is an adventure with all sorts of hidden treasure and more answers than the number of Solomon's wives or the ways of writing tribal lays. On the practical side, and it is folly to ignore the practical side, the student learns that you do not cure men of their peculiar ailments by a pill, but by understanding them. And that is an art, high and troubled, not a pretty science which you can learn in your third year, and find in a big book, on page 273.

You do not find out about men and their fear of God and animals, bombs and themselves, in any big technical treatise or on any page. The best doctors know that, and so in their way do the best English teachers. In spite of distraction, boredom and fear they think of you as men, and temper their sharp winds to your naked sides. They know that you are not ruled by mechanical laws but by apparently insignificant things, like the sound of the surf, or a chance oath heard in a crowd, or a phrase in a sonata or a horse going over a gate like a poem. These are the things literature is about and the things men are about. It is for things like this and the perception of their value that pre-medical students come to University College three times a week to sit in a stuffy room and talk about Shakespeare or Dickens or Shaw. I must say you do pretty well.

ENCEPHALITIS

ROBERT G. ARMOUR, B.A., M.B., F.R.C.P. & S. (C.)*

THE DISEASE ENCEPHALITIS or encephalo-myelitis as it is best called (rather than to expand the name into an impossibly clumsy length to include the meninges, nerve roots, and peripheral nerves) over recent years, has become more and more prominent, and probably more common, if one's failure to recall many cases thirty or forty years ago should indicate that they did not occur then.

The whole subject is in need of clarification at the present time on account of the varied clinical phenomena in different cases, and because of the incomplete knowledge we possess.

It is my purpose in this communication to direct special attention only to those forms apparently associated with some of the commoner infectious diseases.

It has been thought by some that this association exists only with the infectious diseases caused by viruses: measles, german measles, mumps, chicken-pox, influenza, occasional cases of the common cold, and another recently coming into prominence, infectious mononucleosis, but it is suggested that involvement of the nervous system has apparently occurred in scarlet fever, Sydenham's chorea, diphtheria and whooping cough, details of suggestive cases being later recorded. In the course of any one of these infectious diseases, cerebral, cerebellar, mid-brain, or spinal cord symptoms may make their appearance. In addition, there may be frank meningeal signs, or a routine lumbar puncture may reveal a pleocytosis of from less than one hundred to three or four hundred cells per cubic millimeter. Also, though it would not seem that xanthochromia is as common in this type of encephalitis as in the so-called Guillain and Barre syndrome, yet the total protein may be appreciably raised. Elevation of temperature may vary from little or none to a hyperpyrexia fatal in itself, in the latter case possibly from paralysis of the heat regulating centre by the location of the process.

It would not seem that any particular form of nervous involvement characterizes the association with any given infectious disease, though it would appear that convulsions occur in a greater proportion of infectious mononucleosis than in the other infectious diseases. On the whole, however, the predominance of symptoms arising from one part or another of the nervous system may be entirely accidental, the encephalitis complicating one infectious disease resembling that complicating another disease. Some of such symptoms are: convulsions, hemiplegia, eye palsies and other mid-brain and bulbar phenomena, transverse myelitis, Landry's syndrome, or an ascending myelitis involving both motion and sensation, peripheral neuritis, including that syndrome called acute infective polyneuritis in which a double facial paralysis and paralysis of the proximal muscles of the limbs predominate.

The extent and severity of the symptoms vary widely from such a case as one in which only a series of convulsions occurred on one day and no permanent residuals resulted, this being a case of measles, to one with Landry's syndrome

*Associate Professor of Medicine, University of Toronto.

in which the paralysis ascended to the bulb and death ensued from involvement of the respiratory system, in this instance a case of chicken-pox. Another case is one in which an incomplete hemiplegia complicated an attack of influenza. Twelve years later, this case was seen suffering from spastic paraplegia after an attack of subacute pyelitis of several weeks duration.

Can it be that we are dealing with a certain type of individual whose nervous system is more vulnerable to infectious diseases than most individuals? Of this later.

It is important to keep in mind that the likelihood of such complications is not in direct proportion to the severity of the original disease, but rather on the contrary, perhaps more often occurring in the milder cases. Nor do these complications necessarily show themselves in any particular stage of the disease, but occur sometimes in the initial stages and sometimes during convalescence. In the former instance, the development of the encephalitis may indicate an invasion by a more virulent virus. In the latter instance, over-exertion and fatigue, as will be indicated in some case reports, may be the precipitating factors when the infection has been mild.

It can be readily understood that a patient suffering from a mild attack of any of these infectious diseases in any stage, early or late, is unlikely to remain in bed, and perhaps is more likely to resume work prematurely, than one who is or has been acutely ill. There are also those individuals who, belittling the exhausting effects of influenza, force themselves to continue at work when they might better be confined to bed. Whether this theory of the effect of over-exertion is entirely true or not, some case reports are very significant. At what stage the invasion by the virus takes place may be indicated by comparing the pathological findings in the following two contrasting cases:

CASE 1: A boy of twelve years of age had had an attack of mumps of apparently average severity.

On the first day on which he was allowed out, a warm, sunny Spring day, he made an excursion of about three or four miles on his roller-skates. The doctor who had been in attendance on him, was looking out of a window across the street, and saw him on his return fall as he stooped to remove his roller-skates. The lad fell a second and a third time as he made repeated attempts to remove his skates, but on no occasion seemed to strike his head, and certainly there were no bruises on it. When the doctor reached him, the boy was violently dizzy and could not stand unaided. When he reached the hospital he was unconscious and exhibited a gross spontaneous nystagmus of both eyes. He died of respiratory failure within forty-eight hours of his fall. Histological sections of his mid-brain showed well developed cuffing or mantling of the blood vessels.

From the well developed pathological picture one might conclude that the encephalitis had been in existence for some time, but without giving any appreciable signs or symptoms until relative over-exertion had been performed.

CASE 2: A young woman in her early twenties developed measles, and in the early stage, and not having performed over-exertions, developed an encephalitis of the diencephalon as indicated by a hyperpyrexia of 106°F. or higher, and a tachopnea of 60 respirations per minute.

She died within three or four days of the onset of the disease and at autopsy microscopic findings consisted of no more than congestion and edema.

This would appear to have been a very virulent infection.

In recent reports on encephalitis complicating acute infectious mononucleosis, it is recorded that the encephalitis has preceded the development of the typical blood picture by as much as three weeks.

The evidence seems to indicate that

the encephalitis is potentially present early in the primary disease. It may in itself be severe enough to cause symptoms in the initial stage or, in other cases, presumably, is brought to the surface by exertion.

CASE 3: A youth in his teens with measles had a series of convulsions on the first day of the clinical appearance of measles.

CASE 4: A man in his thirties, noticed the first spots of chicken-pox on Monday. He spent four days in bed and resumed work loading cartons of soft drinks on trucks on Friday. The next morning he tripped as he went into the bathroom. A rapidly ascending myelitis developed and he died on Sunday morning.

The importance of realizing the danger of exertion in infectious diseases is what I should like to emphasise, this being preventable, though we are at present helpless in the occurrence of a virulent infection. For example, a farmer's wife reported to the author a few summers ago that her daughter had chicken-pox, but "was not too sick to hoe potatoes." In spite of being warned of the danger, that same woman, later in the summer, reported her son as having measles, but "not too sick to run the reaper."

To deal extensively with the nature of these viruses is not the purpose of the writer, it being quite beyond his sphere. Perhaps exact knowledge of the nature of the viruses is not yet very common knowledge. Whether the viruses causing these complications are all identical has not been determined. It has been suggested that the viruses of some of the exanthemata have neurotropic properties.

Bacterial toxins having an effect on the nervous system has not been proved. The allergists will, of course, have their say.

The possibility of infectious diseases of bacterial origin causing encephalitis has been disputed, but it would appear that certain diseases such as diphtheria and typhoid fever can cause degenerative diseases in the blood vessels of the brain, as elsewhere, and so give the clinical appearance of encephalitis.

The following case report might indicate the vulnerability of the nervous system in some individuals to any infection:

CASE 5: A young married woman lost her first baby by miscarriage late in pregnancy. Her next two and only other, children died of amaurotic family idiocy.

Two other members of her family suffered from organic nervous conditions, her father from Meniere's syndrome, and a sister from some nervous disease at present not remembered. Her husband was strong and healthy and had one healthy child by a previous marriage.

The patient herself, a few years ago, contracted a very mild attack of scarlet fever which was not diagnosed until her hands began to peel. Almost at the same time she developed a condition closely resembling disseminated sclerosis, but through ten or fifteen years it made little progress and she never had a remission. It is suggested that the occurrence of amaurotic family idiocy in at least two of her children might indicate a lessened resistance in her nervous system to the effects of infection.

Two cases of Sydenham's chorea may be mentioned here:

CASE 6: A boy of nine developed chorea on his left side years ago at a time when we were not seeing epidemic encephalitis.

As a matter of interest it might be mentioned that, with this chorea, he lost his speech and it was found that his mother and grandmother had been left-handed.

The subsequent history of the case was that he developed epilepsy and was confined to the Ontario Hospital, Orillia, as a mental defective.

CASE 7: The second case was brought to the writer as an epileptic girl of thirty-four suffering from generalized grand mal attacks.

As the attacks became milder and less frequent under treatment, they took the form of transient aphasia accompanied by transient paralysis of the right hand, but no convulsive element.

An air encephalogram revealed a considerable degree of atrophy of the left frontal lobe, and then further investigation unearthed a history of right sided chorea at four years of age.

Such cases of encephalo-myelitis complicating scarlet fever and chorea are probably due to vascular damage, rather than to virus infection but they are recorded to emphasize the dangers of some childhood diseases that are often regarded as trivial.

We have no form of treatment for encephalo-myelitis other than rest and symptomatic medication. The sulphonamides and penicillin do not influence them favourably, and possibly the administration of these might set up reactions that would be prejudicial to the patient.

This may seem to be a summary way of dealing with treatment, but we are as yet somewhat in the dark as to the exact nature of the process which constitutes encephalo-myelitis other than those cases complicating the bacterial diseases. It is only an assumption, though a good one, that they are due to viruses. Whether the condition should be regarded as inflammatory, as is implied by the suffix "-itis," rather than toxic or degenerative, is not certain.

We recognize a demyelination in some cases *post mortem*, and this is regarded as the characteristic pathological process of perhaps all cases; but what brings this about, and what has been the state of affairs in those cases that have died before this process has become established?

What is the point of entry of the noxious agent? By what method does it spread? Where does it act?

At one time the cuffing or mantling of the blood vessels was interpreted as perivascular inflammation. It is now thought that these cells are scavenger cells, produced to dispose of the degeneration products of the myelin. That they are seen in such profusion about the blood vessels may only mean that they are produced there.

It is usually thought that the demyelination indicates that the encephalitis is a process limited to white matter. Is it possible that the primary process occurs in the cell bodies of the neurons, and that the demyelination is secondary to this?

The writer makes no effort to pass final judgment on any of these matters, but hopes to stimulate greater interest and further investigation into a very important sphere of Medicine.

AND AFTER INTERNING, WHAT?

J. B. J. McKENDRY, B.A., M.D.

A RECENT GRADUATE nearing the end of his junior internship is undoubtedly perplexed by the numerous fields of specialized study which he might enter. The possibilities could be tabulated as follows:

1. He may enter directly into some administrative, research, public health, or industrial field, though generally, a short time must be spent first in specialized training.
2. He may have decided already to become a specialist and—
   a. begin training in that field immediately or
   b. take a year in one of the basic sciences prior to beginning training in the chosen specialty.
3. He may:
   a. become an assistant to a specialist in the specialty in which he intends to train, or
   b. begin general practice independantly, or
   c. become an associate of or an assistant to a general physician and surgeon.

The advantages of 1, 2 and 3*a* are well known. It is about 3*b* and 3*c* that I wish to write.

Sit back for a moment and decide to become an assistant to a general practitioner, or to establish a practice of your own.

You can find an opening in the city where the University from which you graduated is located or in some similar large urban area where you can attend lectures, seminars, pathological conferences, and clinics as your time allows. The advantages of these are self-evident. On the other hand you may choose a distinctly rural area where none of these opportunities are to be had but which too has advantages perhaps you have overlooked.

Suppose you decide to locate, let us say arbitrarily, two hundred miles from the nearest large medical center. If you are fortunate, there may be a hospital in the district and that is a distinct advantage. You may now, "with fear and trembling," consider yourself weaned from your Alma Mater and about to apply some of the principles learned in undergraduate and internship days.

The first thing you learn is that primarily you are not dealing with diseases but with people. To date, you have been well schooled in history taking, physical examination, and certain laboratory procedures. In addition to this, there must be developed a "doctor-patient" relationship whereby the patient regards the doctor as a friend and advisor. A patient will meet you on the street some day and say, "Doctor, that cough mixture has certainly helped my boy," and back in your mind you know the cough has been sufficiently investigated. In his next breath, he says, "Oh, by the way, Doctor, I'll be bringing you over a taste of the fish we caught last night if you care for some." You thank him and must now hurry to the hospital to see why Mrs. Jones, a primipara, who has been fifteen hours in labour, is still only three finger's dilated!

Many of your calls will be twenty or thirty miles from the hospital and good

judgment is necessary in assessing the case—whether you should bring the patient back to hospital, whether you should outline treatment with medication to be given at home, or whether you have time to transport a patient to hospital as in the case of a patient in labour. Into one of these decisions must go all of your own careful and unassisted reasoning. A sense of independence is automatically developed.

It is easy, in the large training hospitals, to ask a nurse to go to Central Supply for an interstitial or cut down set but many small hospitals do not stock these. A little planning and a knowledge of equipment available will in most cases overcome many difficult situations. Resourcefulness is always in demand.

Then, too, one develops a "reasoned approach" to each problem. For example, a patient, Mrs. X, goes to Dr. Y to consult him about a very mild case of hives because of the associated itchy discomfort. Says Dr. Y, "Oh yes, Mrs. X that is hives all right. I think this prescription will help you." (e.g. Calamine oz. iv with phenol min. xv.) The hives increased and the itchiness was helped very little, so Mrs. X reasoned to herself "because the hives are increasing, this medication is not right, I'll see Dr. Z." Now, Dr. Z when speaking to Mrs. X asked her about food allergy, prescribed in addition benadryl and the hives cleared. Mrs. X classifies Dr. Z a good doctor, Dr. Y a poor doctor, when actually, in this instance, both are blameworthy. Neither Dr. Y nor Dr. Z took time to explain to Mrs. X that often hives run a mild course and calamine lotion alleviates most of the itching but occasionally a more severe attack is encountered and further treatment is necessary. In other words a planned approach (known to the patient) is developed in the treatment of each patient and sufficient follow-up done so that you are aware of the final outcome.

Then, too, for the first time you feel that you are making some definite contribution to a community. Until now, you depended on the decisions of staff men, residents, and senior interns, but now you are the one who makes the decisions and has the full responsibility for treatment.

Presently, your year or two in general practice is up. If you have made up your mind that you want to study a specialty you do not need to worry about the current saying, "once you go out in general practice you'll never come back for further study." Many have. If you decide you like general practice there are many openings available and, furthermore, most universities are sponsoring short refresher courses for general practitioners. Perhaps your associate will want you as a partner.

During the time spent in general practice you have become a specialist in your knowledge of one or two of the chief industries of the locality, perhaps railroading, for example, and the following will illustrate its usefulness. Suppose you returned as planned and studied internal medicine with special emphasis on cardiology. Five years later, a general practitioner refers a patient to you with minimal cardiac failure. Of course, you will take an electrocardiogram—all cardiologists do—and you will send the doctor a complete report (within twenty-four hours after seeing the patient, because you well know how the family keeps phoning to see if you have yet received the specialist's reply) which might read as follows:

Place.
Date.

Dr. A,
Place.

Dear Dr. A.

Re: Mr. T. J. Doe

Enclosed please find a copy of my physical examination and laboratory investigation which I expect differs little from yours, as well as a copy of the ECG report.

As Mr. Doe is the only wage earner in his family, we shall have to do everything possible to keep him gainfully employed. He is a railway engineer, well up on the seniority list for his division and, therefore, will have priority on most runs.

I do not think it advisable that he take a passenger run because of the great responsibility, nor the yard engine because of the constant shifting back and forth of the throttle, but would advise a run such as the way-freight where he would be assured of more or less regular hours with time off for meals and sleeping hours at night. Pool freight, of course, is too strenuous and meals and sleep are too irregular.

For his immediate use I would prescribe.....

Yours truly,

Dr. B.

General practitioners invariably appreciate the more practical aspects of consultation.

So, if your plans are undecided and a suitable assistantship is available, "there is experience to be had for the asking" in general practice.

A PROBLEM IN DIAGNOSIS

ROSS K. DOBSON, 4T9

PRESENTATION OF CASE

G.M., A THIRTY-THREE YEAR OLD white male was admitted to the Toronto Western Hospital at 6:30 p.m. on November 8, 1948, complaining of abdominal pain, nausea and vomiting for six hours.

He had been in good health until the day of admission. During lunch, he was suddenly seized with a severe pain, felt transversely across the abdomen above the umbilicus, which rapidly became worse and reached its maximum intensity about 15 minutes after its onset. Acute nausea coincided with the onset of this pain, and was soon followed by vomiting. The pain was severe and boring, did not fluctuate in intensity, did not radiate to the back or lower abdomen, was aggravated by breathing but not by bodily movement, and was slightly relieved by sips of ice cold water. A sharp pain also aggravated by breathing was felt simultaneously in the left shoulder tip area. During the six hours between the onset of the pain and his admission to hospital, the patient alternately paced the floor and lay quietly, but could get no relief. Vomiting occurred intermittently, the vomitus at first consisting of food particles and later of greenish bitter fluid.

The patient was an unmarried factory engineer who had no past illnesses of any significance and whose family history was non-contributory. He had a head cold with a cough during the previous week. His exercise tolerance was excellent and he had no previous symptoms suggestive of coronary artery disease. For the past 1-2 years, he had experienced a feeling of fulness in the epigastrium which was most marked between meals and at bedtime and which was relieved by belching. He had no history of weight loss, anorexia, nausea or vomiting, food intolerance, jaundice, abdominal pain, abnormality of bowel habit or stools, or symptoms suggestive of diseases of the urinary system.

The patient appeared to be a well-nourished, slightly dehydrated male of about forty years of age. He was dyspneic, pale, sweating, restless, and obviously in acute distress. No cyanosis or jaundice was evident. The pulse rate was 72; blood pressure, 130 mm. systolic, 70 mm. diastolic; temperature 100°F. The chest was clear. The heart was not enlarged, and there were no heart murmurs or signs of cardiac decompensation. The pulse was full and regular. The abdomen moved moderately well with respiration. There was no distension or visible peristalsis. In the epigastrium, there was some muscle splinting which could be broken down, and an indefinite area of hyperaesthesia. Throughout the upper abdomen there was very marked tenderness and rebound tenderness maximal in the epigastrium. A small amount of free fluid was demonstrable by shifting dullness. No masses were felt and the liver, spleen and kidneys were not palpable. The hernial orifices were clear and no discoloration of the skin was noted. Rectal examination was negative. He was extremely nervous and apprehensive but the neurological examination was otherwise negative.

The hemoglobin concentration was 100% and the white cell count was 10,000. The urine was highly concentrated and

contained a trace of albumin but was otherwise normal. The vomitus obtained was scanty and bile-stained but never feculent. X-ray examination failed to reveal free air beneath the diaphragm, distended loops of bowel or opacities suggestive of biliary or renal calculi.

SUMMARY. This man was admitted to hospital with a six-hour history of epigastric pain of sudden onset, pain referred to the left shoulder tip area, and nausea and vomiting. He was dyspneic, pale, sweating, restless and obviously in great pain. There was marked tenderness, rebound tenderness and a slight degree of muscle splinting in the epigastrium.

DIFFERENTIAL DIAGNOSIS

The diagnosis of the acute abdomen is a problem requiring the finest degree of clinical judgement. It must be made when the patient is first seen, and therefore without the aid of extensive laboratory investigation. On it depends the immediate plan of therapy, and delay may cost the patient his life.

Perforation of a peptic ulcer is suggested by the sudden onset of prostrating epigastric pain, pain referred to the left shoulder tip, marked epigastric tenderness and vomiting. It is usual, however, for the pain to be replaced by a sensation of soreness and the vomiting to cease after an initial violent bout. During this phase the patient is quite comfortable as long as he remains motionless, the slightest movement causing exquisite pain. This sequence of events is in contradistion to the restlessness, persistent pain and vomiting demonstrated by this patient. The previous history of indigestion is sufficiently vague to be discarded as a point of differential value, but it is not uncommon for an acute ulcer to be symptomless until perforation occurs. The absence of abdominal rigidity, however, eliminates the possibility that an ulcer has perforated into the general peritoneal cavity, because the rigidity accompanying such a catastrophe is unique, being complete, generalized and impossible to break down. Tenderness of the pelvic peritoneum on rectal examination is commonly demonstrable.

Acute pancreatitis is suggested by the characteristic epigastric direct and rebound tenderness in the absence of abdominal rigidity. The persistent, severe pain of sudden onset, distributed transversely across the upper abdomen, with pain referred to the left shoulder tip also supports this diagnosis. Persistent vomiting and retching is usual, and is accompanied by a slight rise in temperature and a relatively normal white blood cell count.

Acute intestinal obstruction high up in the small bowel, such as might be caused by adhesions, congenital bands, strangulated external or internal herniae or mesenteric thrombosis or embolism often has an onset similar to that described by this patient. The absence of a previous abdominal incision and the negative findings on examination of the inguinal and femoral canals rule out the two most common causes of acute intestinal obstruction. In addition, the pain is usually crampy, and is periumbilical rather than epigastric in location. Tenderness is not a feature of the early stages. Visible peristalsis is pathognomonic if present and distension, although often slight, is usual. X-ray examination usually shows distended loops of small bowel.

Although *acute cholecystitis* would explain many of the symptoms and signs in this case the pain is more usually confined to the right upper quadrant of the abdomen, seldom crosses the midline

and could never radiate to the left shoulder tip unless rupture of the gall bladder occurred. The point of maximum tenderness is consistently in the right upper quadrant and the gall bladder may be palpable. An elevation if the white blood count is usual.

The pain of *coronary occlusion* is frequently referred to the epigastrium and this may be its only area of localization. Thus the history of sudden epigastric pain, breathlessness, nausea and vomiting is not incompitable with this diagnosis. The association of abdominal pain with true abdominal tenderness, however, indicates an intra-abdominal rather than an extra-abdominal lesion, and the than an extra-abdominal lesion. The radiation of pain to the shoulder tip and the absence of the characteristic radiation of pain of coronary occlusion to the neck or arms further exclude the diagnosis.

CLINICAL DIAGNOSIS

Acute pancreatitis.

CLINICAL COURSE

With conservative treatment the patient's general condition remained serious during the first 36 hours and then rapidly improved so that by the fourth day of his illness he was comfortable and almost free of pain. The patient's temperature paralleled his general condition, being elevated to 100°-102°F. during the first four days and normal subsequently. The white blood cell count remained within normal limits throughout. The serum amylase activity, which was 40 units (normal: less than 25 units), when estimated a few hours after admission, returned to normal on the second day and remained so.

After ten days, the patient's condition was excellent and radiological examinations of his gastro-intestinal and biliary systems revealed no abnormalities. He was discharged on November 25, 1948, seventeen days after admission.

The uncomplicated recovery shown by this patient is compatible with the clinical diagnosis of acute pancreatitis. The degree of elevation of serum amylase activity also supports this diagnosis, but cannot be considered pathognomonic.

ACKNOWLEDGEMENT

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THE ROLE OF PROGESTERONE IN THE MAINTENANCE OF PREGNANCY

NORMAN C. KERBEL, B.A., 5T1

IT IS GENERALLY conceded that about ten per cent of all pregnancies end in spontaneous abortion, or miscarriage, which causes a greater wastage of actual and potential citizens than any disease. It is no surprise, therefore, that this aspect of obstetrics has attracted a great deal of attention and has been thoroughly and painstakingly reviewed. The exact role of progesterone in maintaining pregnancy is far from being established, but this article is offered as a brief summary of the mass of pertinent literature.

ESSENTIALITY OF THE CORPUS LUTEUM

It has been repeatedly shown that the corpus luteum is essential for the maintenance of pregnancy in various animals. In the mouse, for example, Parkes (1) has shown that if the right ovary is sterilized by X-ray and the left ovary is removed between the eleventh and seventeenth days of pregnancy, the gestation is interrupted. However, if the sterilized right ovary is removed and the functioning left ovary remains, the pregnancy is maintained to term. Similarly, ablation of the ovaries terminates pregnancy in the opossum and rabbit anytime during its course. The relation of the corpus luteum to the maintenance of pregnancy has recently been thoroughly studied in the rat by Zeiner (2). He showed that the average duration of pregnancy after ovariectomy was more than 108 hours; however, in all cases, the pregnancy was terminated before term.

In the horse and the cat, removal of the ovaries can be effected at the end of the second trimester without interruption of the pregnancy. In the guinea pig, both ovaries may be removed as early as the end of the first trimester without interruption of gestation. In the *Rhesus* monkey, Hartman and Corner (3) found that the corpus luteum of pregnancy may be removed as early as the twenty-fifth day without disturbing the gravid state.

In the human, as in the monkey and the guinea pig, it is apparently safe to remove the corpus luteum quite early in the pregnancy. Sturgis (4) suggests that it may be removed after the second month without interrupting the pregnancy, while removal before the second month results in abortion in 10 - 33% of the cases. Pratt (5) has reported cases in which castration as early as 20 days after the onset of the last menstruation failed to disturb the course of the pregnancy.

When abortion occurs after corpus luteum ablation or ovariectomy, the cause is deficiency in progestin according to the evidence accumulated from experiments performed in those animals in which a corpus luteum is necessary throughout pregnancy. For example, in the rabbit Allen and Corner (6) maintained the pregnancy in castrated rabbits with a crude extract of sows' corpora lutea. Progestin also allows the pregnancy to proceed normally in the castrated rat, mouse, and squirrel.

THE PLACENTA AS A SOURCE OF PROGESTERONE

The question arises as to why some species require an active corpus luteum throughout gestation, whereas others can be deprived of it at varying times

during pregnancy. All evidence seems to indicate that there is an extra-ovarian source of progesterone and recent experiments point to the placenta as being that source. An observation of limited value in this connection is that progesterone is found in the placenta. This does not necessarily indicate that the placenta produces the hormone. It may be merely the storage organ.

Of greater interest and importance are the studies with retained placentae in the rat by Kirsch (7), and in the mouse by Newton (8). These workers showed that five days after removal of the fetuses, the endometrium and myometrium are still typical of pregnancy if the placentae have not been disturbed. Furthermore, the placentae are delivered at full term. These effects could be due to one of two alternatives: either the placenta is an endocrine gland whose secretion is responsible for maintaining the gravid state, or the distended uterus, by means of nervous stimuli, is responsible. To test these alternatives, Newton and Lits slit the uterus of pregnant mice whose fetuses had been removed but whose placentae had been retained. This procedure, which would certainly have been expected to eliminate tension, did not interfere with the effects of the retained placentae mentioned above.

Other experiments which would indicate that the placenta produces progesterone are those of Haterius (9). He showed that a spayed pregnant rat from whom all but one of the fetuses had been removed would carry to term. The explanation is that the retained placentae produced enough progesterone to take care of one fetus; that is, there was a high placenta: fetus ratio. However, castration, when this ratio is unity, results in abortion as indicated previously.

Thus we see how the theory evolved that the placenta is an endocrine organ and that in those animals in which the corpus luteum is not essential throughout pregnancy, the placenta assumes the role of supplier of progesterone. Corner, Bartelmez and Hartman have provided evidence of a definite histological change in the corpus luteum of the monkey which begins about the twenty-first day of pregnancy and is always completed by the twenty-fifth. It will be recalled that this corresponds to the beginning of the period when it is safe to castrate a pregnant monkey. In all probability, the histological change marks the time when the corpus luteum ceases to be indispensible and the placenta takes up its endocrine function.

It is important to note that a similar mechanism probably operates in the human and that the highest incidence of abortions occurs in the critical period of the switchover. This critical interval varies with different individuals and even in the same individual during successive pregnancies but generally, it takes place between the end of the second month and the fourth month.

MODE OF ACTION OF PROGESTERONE

Having thus far indicated the importance of progesterone, it is now our task to determine the mode of action of the hormone. Several have been suggested and all, one, or none may be important. Evaluation of the evidence is made difficult by the fact that apparently equally reliable experiments point to opposite conclusions. The well documented evidence proving that progesterone is an essential factor in the initiation of pregnancy will not be considered.

The most commonly suggested role

for progesterone is that of a uterine sedative. The knowledge concerning this effect dates back, as is the case in numerous physiological problems, to the investigations of Dale who reported that the uterus of a non-pregnant cat does not respond to adrenalin or hypogastric stimulation like that of a pregnant cat which contracts under these stimuli. The factor which is responsible for this difference is probably the presence of increased amounts of progesterone.

The oft-quoted investigations of Knaus (10) carry great weight and are worthy of a full discussion because of their importance. This author found that uterine responses to pituitrin vary greatly at different stages of gestation in the rabbit. At full term (32 days), only a minute quantity is required to cause delivery of the whole litter within ten minutes; whereas, on the twenty-ninth day, ten times as much pituitrin is required to produce the same effect. Between the twenty-eighth and twenty-ninth days a sudden change occurs in the responsiveness of the uterus to pituitrin so that no amount of posterior pituitary lobe extract can induce parturition on the same day as the injection. During the first half of the pregnancy, the rabbits might be said to be entirely unresponsive to pituitrin although, as gestation progresses, the animals become more and more responsive. Subsequent studies make it clear that the progesterone which is present in increased quantities during pregnancy protects the uterus from the stimulating action of pituitrin.

Falls, Lackner and Krohn, in a well known experimental study on women shortly after parturition, found that small doses of progesterone protect the uterus from the oxytocic action of pituitrin. This inhibitory effect lasts for several hours.

It should not be supposed that the suggestion that progesterone acts as a uterine sedative goes unchallenged; indeed, in recent years evidence has accumulated that progesterone may increase uterine motility. This controversy has not been resolved as yet and it is one of the main problems which beclouds this field of endorcinology. The work of Moir (11) may be quoted to support the thesis that progesterone, in its own way, is a uterine activator. He found that there is a pattern of uterine contractions characteristic of the follicular (estrogen) phase and another pattern characteristic of the luteal (progesterone) phase of the menstrual cycle. During the latter phase, when the uterus might be expected to be quiescent, Moir found that the myometrium undergoes contractions which are increased in amplitude but greatly decreased in frequency.

Novak (12) has recently reviewed some of the evidence presented above and concludes that the investigation and opinion of most workers in the field points to the probable correctness of Knaus's viewpoint. It is typical of the confused state of affairs in this problem that Bender (13) reviewed the same literature and came to a diametrically opposed conclusion.

Other effects have been attributed ot progesterone and one of the most reasonable of these is the inhibition of ovulation. The importance of this in relation to the maintenance of pregnancy is obvious. It is reasonable to suppose that abortions would be frequent in cases of superfetation. However, Stander in his brief review of the literature concludes that no instance of true superfetation has ever been recorded and

attributes this phenomenon to the cessation of ovulation. This action of progesterone has been well established by a multitude of experiments. Among those which might be mentioned are the investigations of Loeb who noticed that extirpation of the corpora lutea from a guinea pig's ovary at an early stage in the estrus cycle led to ovulation before the date at which it would normally occur. Even during pregnancy, removal of the corpora lutea was followed by ovulation. From these facts, Loeb concluded that ovulation is inhibited by the secretion of the corpora lutea. Injections of crude extracts of sows' corpora lutea in the rabbit and the guinea pig inhibited ovulation shortly before coitus when it normally would have taken place. This action of progesterone seems to be mainly indirect and depends on its capacity to check the supply of follicle stimulating hormone from the pituitary and so to inhibit maturation of follicles.

There is fragmentary evidence that the hormone of the corpus luteum increases and maintains the fetal-maternal vascular connections and in general enhances the blood supply to the uterus. Champy and Keller (14) indicated that corpus luteum extract will produce vasodilatation and hyperemia of the uterus. Selye and McKeown (15) in a study of artificially produced placentoma in the rat, found that the blood sinuses that form in the placenta are purely maternal structures induced by progesterone. More recently, Hechter, Krohn and Harris (16) have observed that progesterone increases the permeability of the uterine capillaries.

CLINICAL EXPERIENCES

With all that has been said in the previous paragraphs, one might reasonably expect that progesterone would have a very beneficial effect in maintaining pregnancy in clinical cases of threatened and habitual abortion. Indeed, soon after progesterone preparations became available, numerous clinical investigations to test its efficacy in these cases were undertaken and at the beginning the reported results were almost uniformly excellent. In recent years, however, disappointment in the value of progesterone therapy has been expressed by many clinicians; nevertheless, it continues to be used in many of the best obstetrical clinics. The attitude of the clinician varies between that expressed by Krohn and Harris who feel that anhydro-hydroxy progesterone (an orally active derivative of progesterone) gives most satisfactory results, and that expressed by Peterson who found that progesterone may be harmful and his results have been better since he gave up using it. Hertig and Livingstone (17), in a most interesting and valuable paper have tabulated the data on the treatment of threatened and habitual abortions that were published in the ten year interval prior to 1944. They list about thirty communications dealing with hormonal therapy in abortion and it would be impossible to discuss each of these in the space available; the reader is referred to their comprehensive paper.

An investigation of great importance which will possibly have a unifying influence on the whole field of progesterone therapy in abortion has recently been completed by Bender (13). In order to appreciate the significance of this author's work, a few words must first be said about the metabolism of progesterone.

Browne, Henry and Venning have established, with a fair degree of certain-

ty, that pregnanediol is the urinary excretion product of progesterone by the following experimental observations: (*a*) Pregnanediol excretion coincides with the period of corpus luteum activity in the ovular menstrual cycle. (*b*) In normal pregnancy, when the corpus luteum persists, the excretion of pregnanediol in the urine also persists. (*c*) Administration of progesterone is followed by the appearance of pregnanediol in the urine.

There is a pattern of urinary pregnanediol excretion in pregnancy despite individual quantitative variations. Up to the ninth week after the end of the last menstrual period the excretion usually slightly exceeds that of the height of the luteal phase of the ovular menstrual cycle. After this time there is a sharp rise in pregnanediol output which reaches a maximum two or three weeks before term, when a decline sets in. The important point is that if progesterone production, as indicated by pregnanediol excretion is not maintained at its normal high level, abortion will follow. These results have been extended and amplified by Hain who enumerates some of the cases described in the literature in which a high pregnanediol excretion (and therefore a presumably sufficient progesterone supply) were associated with abortion and wisely considers the possibility of faulty utilization in such cases.

Arguing from this evidence, Bender (13) is of the opinion that cases of threatened abortion should be divided into two groups: (*a*) Those accompanied by evidence of progesterone deficiency, and (*b*) those not so accompanied. Progesterone therapy would then be limited to cases coming within the first group. The distinction between the groups can be made by means of Bender's rapid quantitative urinary pregnanediol test, a modification of the Guterman test. Bender's results in the series reported were extremely good.

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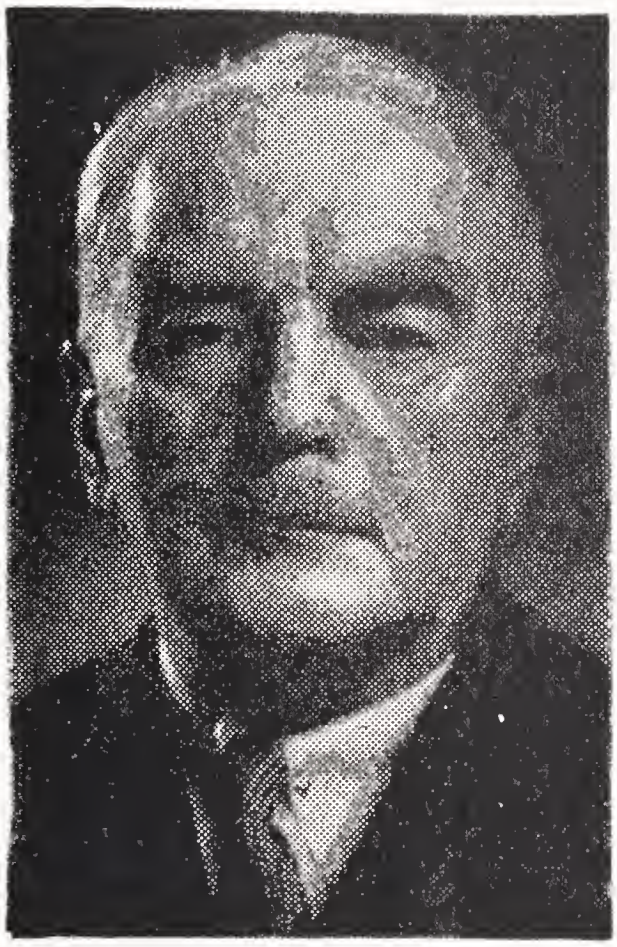

DR. G. E. RICHARDS

In our midst, he lived—a student and a teacher; a keen observer, active in medical practice and research; at all times, a friend and a guide.

From our midst, he passed.

He lives on among us—through his discoveries and his teachings, and ever in our memories.

"So when a great man dies,
For years beyond our ken,
The light he leaves behind him lies
Upon the paths of men."

—Longfellow.

DR. GORDON RICHARDS

DR. GORDON EARLE RICHARDS died at Toronto on January 13, 1949, at 63 years of age. While he had been quite seriously ill for the past number of months, his death was a great shock to his friends, his associates and his pupils.

Dr. Richards was born at Lyn, near Brockville, Ontario, on the 15th of March, 1885. He was the son of the Reverend J. J. Richards and Anna Paul. He attended Athens High School near Brockville and was graduated from the University of Toronto with the degree of Bachelor of Medicine, and gold medalist of his class, in 1908. Following graduation, he practised for some years in Prince Rupert and later in Stewart, British Columbia, following which he moved to Vancouver, where he practised Radiology from 1912 to 1915. Early in 1915 he proceeded to England, where he joined the Royal Army Medical Corps and served as Radiologist to No. 21 General Hospital, R.A.M.C., during the Gallipoli Campaign. Returning to Toronto, he assumed duties as first Medical Radiologist to the Toronto General Hospital on the 1st of January, 1917, with which institution he has been intimately associated since that time.

At the time of his death Dr. Richards was Professor of Radiology, University of Toronto, Attending Radiologist-in-Chief, Toronto General Hospital, Director of the Ontario Institute of Radiotherapy and Managing Director of the Ontario Cancer Treatment and Research Foundation.

In 1920 he set up the first high voltage X-ray treatment machine for cancer therapy in this country. In later years his whole interest was cancer therapy by radiation, in which field he was outstandingly successful and made many contributions to medical radiological literature, and the Ontario Institute of Radiotherapy will stand as a memorial to his great work in this field.

Dr. Richards was the recipient of many honours. He was one of the early Fellows of the American College of Radiology, was Vice-President of this Organization and has acted for many years as Councillor for this body. In 1947 he was invited by the Faculty of Radiologists of London, England, to deliver the Skinner Lecture on cancer of the breast. This was the first time that this honour had been conferred on anyone outside the British Isles or Europe. In 1948 Queen's University, Kingston, conferred upon him the Honorary Degree of LL.D. for his outstanding work in the science of radiation and in cancer therapy. In 1947 he was made an Honorary Member of the Royal Society of Medicine. Dr. Richards was responsible for the organization of the Canadian Association of Radiologists in 1937, an organization comprising over ninety percent of the radiologists in Canada, both French and English-speaking.

His great fortitude and zeal are characterized by the fact that, knowing he had only a few months to live, he carried on his great work until in December, 1948, he became bed-ridden.

In the death of Dr. Richards the University has lost a great teacher, the community a great worker and the world an outstanding warrior in the fight against cancer.

A. C. SINGLETON,
Professor of Radiology.

HUMANISM AND MEDICINE

H. B. VAN WYCK[1]

PART V

HELLENIC MEDICINE

THE SEMI-MYSTICAL therapeutic lore of the near East was known to the Greeks of the Fifth Century, and many of the pioneer thinkers cited in the preceding part contributed to its more scientific development. Empedocles was a pioneer in public health and is said to have freed a town of pestilence by drainage of a neighboring swamp. Democritus, a contemporary of Hippocrates, studied the anatomy of animals and the physiology of reproduction. The gymnasts, who were devotees of practice rather than theory, acquired skill in the treatment of injuries; and the growth of the priesthood in the temples dedicated to the semi-mythical Aesculapios also added to a rudimentary interest in diet, baths and exercise. These influences on the development of medicine—religious, philosophic and athletic—formed the early education of the "Father of Medicine," Hippocrates of Cos, born in 460 B.C.

Little of fact is known about his life—much that is obviously legendary has come down to us, but he is a credible figure; and through his works, the so-called Hippocratic collection, we can hear the voice of the Father of Medicine speaking with honesty and humanity and often with a strongly modern idiom. He travelled widely and practiced in Thrace, Thessaly, Delos and Athens, dying almost a centenarian at Larissa. His early training was among the Asclepiads, a temple cult of priests who practiced the art and maintained the tradition of the primitive and superstitious medicine of the time. It would appear that Hippocrates, early in his career, rejected these traditions and brought medicine from within the temple out into the light of scientific scrutiny. The many incidents associated with the Hippocratic legend are perhaps part of the popular fiction which tended to grow up about the forceful figures of that day. As examples, one could cite his professional visit to Democritus and his consultation on Perdiccas, King of Macedonia. It is strange that Plato refers to Hippocrates only twice and Aristotle only once; and yet the Hippocratic writings bring compelling evidence of their origin in the life of a personality of great originality and force.

The Hippocratic collection of writings began to accumulate and circulate early in the Hellenistic period at the Alexandrian medical schools. The authenticity of many of these writings has been a matter of debate. The earliest manuscript extant dates from the Ninth Century A.D.; earlier papyrus fragments exist. In the one hundred works that are found in the collection, many are obviously spurious and of later dates. In the smaller number that appear genuine, the true Hippocrates of tradition appears—the clear-eyed observer, unprejudiced by tradition or preconception, the first physician to separate medicine

[1]Head of the Department of Obstetrics and Gynecology.

from philosophy. Medicine became inductive. The quack with a system relies on deduction only and hopes for spontaneous results and statistical probability to secure his thesis. It must have been difficult in those early days to be an independent objective observer of a most important human problem—illness—in which inductive methods of investigation were and still are too rarely in use. Indeed it can be said of the whole Hippocratic collection that superstitions and irrational supernaturalism have been laid aside. The author or authors consistently maintain the allegiance to the idea of natural law.

In the writing known as *The Sacred Disease*, which is a treatise on epilepsy, there is found, for the first time in the recorded literature of mankind, this rational view of disease. It is remarkable that it should appear in reference to a nervous disorder that modern medicine in its ignorance still terms idiopathic.

"As for this disease called divine, surely it too has its nature and causes whence it originates just like other diseases and is curable by means comparable to their cure. It arises like other diseases from things which enter and quit the body such as cold, heat, the winds, the ever moving and changing things. Such things are divine or not as you will, for the distinction matters not; for all things are alike divine or all are alike natural as you will. All have their antecedent causes which can be found by those who seek them."

Compare this with the references in the New Testament to the "unclean spirit."

The first and third books of the *Epidemics* perhaps reveal the genuine Hippocrates; the famous *Aphorisms* contain the memorable sentences:—

"Art is long and life is short, the time is urgent. Experiment is perilous and decision is difficult. The physician must be prepared not only to do what is right himself, but also to make the patient, the attendant and the externals co-operate."

In reading the record of the past, the maze of error and erroneous conjecture may at times excite the surprise and elicit the interest of the antiquarian; but the student of medical history is mainly occupied with the truth uncovered and the upward trails marked out by the ancients. So far has been noted the clearer tone of honesty and independent judgment in the Hippocratic writings; but now one must note the development of the doctrine of the four humors, the main flaw in the Hippocratic system. This dogma for which Hippocrates was not responsible and which was more fully developed after his time derived mostly from the doctrines of Empedocles, one of the cosmological philosophers. Four elements: air (*Anaximanes*), water (*Thales*) fire (*Heracleitus*), earth (*Xenophanes*), had been successively proposed as the original source of all things and Empedocles substituted for these monistic views a pluralism which included all four. The humoral theory developed out of this synthesis. Blood is moist and hot like air; phlegm is moist and cold like water; yellow bile is dry and hot like fire, and black bile is dry and cold like earth. On the four fluids (or humors): blood, phlegm, yellow bile, and black bile, depended health. If their blending was harmonious (*crasis*), normal health prevailed; but if there was improper blending (*dyscrasis*), disease was present.

These humors also affected the character and temperament of an individual inasmuch as he might be sanguine (*sanguis*, blood), that is cheerful and vigorous; phlegmatic (*phlegma*, slimy mucus), that is, cold and sluggish; choleric (*chole*, bile or anger), that is irritable and

irascible; and melancholy (*melas*, black; *chole*, bile), that is dejected and gloomy.

This fanciful physiology persisted in medical literature down almost to the present but, of course, to-day, it has no relation to scientific fact. Nevertheless, the word humoral still suggests fluid in pathological discussion.

The ideas associated with the old and superseded "humors" however, have taken firm root in our literature in which examples are readily found. The relation of health to temperament appeared especially to the Elizabethan poets; and one finds in *Julius Caesar* the sanguine Antony; phlegmatic Octavius; the choleric Cassius, and melancholy Brutus[10]. When Ben Jonson calls his play *Everyman In His Humor*, he is referring to temperament and propensity, not to comedy. The last speech of Shakespeare's Antony harks back to these old primitive beliefs:

"His life was gentle, and the elements
So mixed in him that nature might stand up
And say to all the world this was a man."

Thus may the discards of science enrich the imagery of letters.

The surgical treatises, for example, *On Wounds Of The Head*, show Egyptian influence but have a modern ring. Such is heard in the description of the trephine operation almost as done today. In the treatise *Concerning Things In Surgery*, whole passages could be transferred with little change to modern textbooks. Hearken to this voice speaking 2,000 years ago:

"Operative requisites in the Surgery are the patient, the operator, assistants, instruments, the light, where and how placed. The operator whether seated or standing should be placed conveniently to the part being operated upon and to the light. Each of the two kinds of light, ordinary and artificial may be used in two ways, direct or oblique."

Again:

"The nails of the operator neither to exceed or come short of the finger tips. Practise using the finger ends. Practise all the operations with each hand and with both together, your object being to attain ability, grace, speed, painlessness, elegance and readiness. Let those who look after the patient present the part for operation as you wish it and hold steady the rest of the body, so as to be all still each keeping silence and obeying each his superior."

Immense importance was attached in these Hippocratic writings to the art of prognosis. The description of the signs of impending death in the *Prognostics* is deservedly famous and to this has been attached the name of the "Hippocratic facies":

"The sharp nose; the hollow eyes, collapsed temples; ears cold, contracted; skin at forehead, rough stretched and parched; colour of face greenish, dusty, livid or leaden' Know then that the end is near".

Compare this with the inimitable imitation in *Henry V*, the scene at the Inn with the sorriest trio of rascals that Shakespeare could invent and the hostess telling of the death of Sir John Falstaff. Shakespeare must have known about the "Hippocratic facies" of impending dissolution:

"For after I saw him fumble with sheets and play with flowers and smile upon his finger ends I knew that there was but one way. His nose was as sharp as a pen and a' babbled of green fields . . . ".

Among the *Aphorisms*, the most famous book of the collection, is much experience that has been confirmed by subsequent generations. Meticulous clinical observation was a new thing. Although Hippocrates had no laboratory, had never seen a human body dissected, had no microscope, no chemistry, never-

[10]Libby: *History of Medicine*, Houghton, Mifflin Co., 1922.

theless he found medicine dying in obsolete temples, left it re-vitalized, and set it upon its high mission. How modern are these Greeks of the Fifth Century B.C.? Why was western man by the Third Century A.D. to slip back into darkness and intolerance for a thousand years? That question will later seek an answer. For the first time, due emphasis was placed on diagnosis. In the *Epidemics* of Hippocrates, forty-two case histories are cited—a monument of a great physician not to be paralleled for two thousand years. Characteristic of his wisdom was his faith in the *vis medicatrix naturae*—the remedial function of nature, a conservative expectancy with the elimination of inept surgery and the use of drugs and fluids as auxiliary to the natural vitality of the body. Hippocrates, as revealed in the more genuine writings, is more modern than most of his successors up to the present century. For the most part impervious to the sway of unproven theory and seeing the general in the particular and the particular in the general, he never failed to focus the centre of his vision on the individual patient.

In the moving and awesome Hippocratic Oath, probably written partly before and partly after his time and yet a symbol of the Hippocratic tradition, posterity may read one of the noblest statements of professional ethics that have ever dignified the pages of history —a document which lifts both the science of medicine and the humanistic attainment of his time to the highest level as yet recorded in the annals of mankind:

"I swear by Apollo the physician, and Aesculapius, and Health, and All-heal, and all the gods and goddesses, that, according to my ability and judgment, I will keep this Oath and this stipulation—to reckon him who taught me this Art equally dear to me as my parents, to share my substance with him, and relieve his necessities if required; to look upon his offspring in the same footing as my own brothers, and to teach them this art, if they shall wish to learn it, without fee or stipulation; and that by precept, lecture, and every other mode of instruction, I will impart a knowledge of the Art to my own sons, and those of my teachers, and to disciples bound by a stipulation and oath according to the law of medicine, but to none others. I will follow that system of regimen which, according to my ability and judgment, I consider for the benefit of my patients, and abstain from whatever is deleterious and mischievous. I will give no deadly medicine to any one if asked, nor suggest any such counsel; and in like manner I will not give to a woman a pessary to produce abortion. With purity and with holiness I will pass my life and practice my Art. I will not cut persons laboring under the stone, but will leave this to be done by men who are practitioners of this work. Into whatever houses I enter, I will go into them for the benefit of the sick, and will abstain from every voluntary act of mischief and corruption; and, further, from the seduction of females or males, of freemen and slaves. What ever, in connection with my professional practice or not in connection with it, I see or hear, in the life of men, which ought not to be spoken of abroad, I will not divulge, as reckoning that all such should be kept secret. While I continue to keep this Oath unviolated, may it be granted to me to enjoy life and the practice of the Art, respected by all men, in all times! But should I trespass and violate this Oath, may the reverse be my lot!"[11]

[11]From *The Genuine Works of Hippocrates.* Translated from the Greek by Francis Adams, William Wood & Co., New York.

ABSTRACTS

DERMATOLOGY

The Use of Brilliant Green in the Treatment of Chronic Ulcers of the Skin. A. W. Feinberg: New Eng. J. Med. **239**, 613-615 (Oct. 1948).

Brilliant green inhibits gram-positive microorganisms, especially staphylococci, *Corynebacterium diphtheriae* and *Pseudomonas aeruginosa*. The dye has been variously used for histological staining, in the treatment of erysipelas and leprosy and, combined with gentian violet and acriflavine, in the treatment of burns. Contrary to past opinion, brilliant green is stable in aqueous solution and can be stored in stock solutions. The author has used brilliant green successfully in the treatment of twenty cases of chronic skin ulcers with uniformly excellent results. The ulcers were cleansed with hydrogen peroxide and alcohol and painted with a 2% solution of the dye in distilled water. This treatment was carried out daily until healing was well under way, usually within 7-10 days. The ulcers were dressed with dry, sterile dressings and the patients were urged to rest as much as possible. The author believes that this form of treatment merits further trial in all types of chronic skin ulcers.

M. G. Wolfish

HEMATOLOGY

The Relationship Between Heparin Dosage and Clotting Time. Jaques and Ricker: Blood **3**, 1197-1211 (Oct. 1948).

The authors, working at Connaught Laboratories, found a linear relation between heparin dosage and the logarithm of the clotting time. With moderate intravenous doses of heparin, the clotting time reaches a maximum in 5-15 minutes.

A test was devised (*a*) to determine the sensitivity of animals to the anticoagulant action of heparin and (*b*) to measure the ability of the body to remove heparin from the circulation. It was observed that in normal animals, anaesthesia with pentobarbitone decreased the coagulability of the blood, urethane had no effect, ether had a variable effect, injection of india ink and evisceration caused a hypercoagulability but nephrectomy had little effect. In assessing the effects of these procedures on the sensitivity of the blood to the anticoagulant action of heparin, it was found that pentobarbitone and nephrectomy had no effect, ether increased it, while urethane, injection of india ink and evisceration markedly decreased it. With none of these tests was any effect observed on the duration of heparin action in the body.

G. L. Ralph

GYNECOLOGY

The Present-Day Status of Noninvasive Cervical Carcinoma. G. A. Galvin and R. W. TeLinde: Am. J. Obs. Gyn. **57**, 15-36 (Jan. 1949).

These workers, since 1940, have been extensively investigating the relation of intraepithelial cancer of the cervix uteri or "carcinoma *in situ*" to invasive cancer. During this time 75 cases of carcinoma *in situ* have been diagnosed from biopsy and in all these cases, the entire cervix or a generous cone was available for complete sectioning. The authors conclude from their study that intraepithelial carcinoma is strictly a histologic diagnosis and should be regarded as indicating one of the following possibilities: (*a*) that the biopsy was taken from the periphery of an advanced cervical cancer; (*b*) that microscopic invasive cancer is present elsewhere in the cervix as was demonstrated in 55 of the 75 cases investigated, or (*c*) that only carcinoma *in situ* is present and invasion has not yet taken place as was found in 20 of the 75 cases. The gross appearance and feel of the cervix should be considered in evaluating each case.

The surface lesion may be relatively dormant for years before developing into clinical cancer, the average age of women with carcinoma *in situ* being 37-38 years, in contrast to the average of 48 years for clinical cervical cancer. Carcinoma *in situ* is, in the opinion of the authors, not a "precancerous" lesion but an early stage of true cancer. Often these lesions are completely asymptomatic but in 58% of these women, a history of some type of irregular vaginal bleeding could be elicited, frequently only of postcoital spotting. In none of these patients did the cervix present the clinical picture of cancer although abnormalities such as cervicitis, erosion, laceration and leukoplakia were diagnosed in the majority.

Miss H. A. P. Marcroft

MEDICINE

Moral Problems in the Practice of Medicine. W. L. Sperry: New Eng. J. Med. **239**, 985-989 (Dec. 1948).

This interesting discussion by the dean of the Harvard Divinity School concerns those aspects of the practice of medicine which are overlooked too easily by the undergraduate, but which loom up as soon as he takes his place as a working member of the profession. He opens up the problems of telling the patient the truth, prolongation of life and euthanasia, and the rivalry between the concrete individual and abstract society. He does not attempt to give a final answer to any of these problems but his comments are thought-provoking.

Miss H. A. P. Marcroft

Anticoagulant Therapy of Coronary Thrombosis with Myocardial Infarction. I. S. Wright, C. D. Marple and D. F. Beck: J. Amer. Med. Assn. **153**, 1074-1079 (Dec. 1948).

This is a preliminary statistical analysis of the first 800 cases studied by the Committee for the Evaluation of Anticoagulants in the Treatment of Coronary Thrombosis with Myocardial Infarction. The patients were almost evenly divided into a control group, which received conventional therapy and a treated group, given conventional plus anticoagulant therapy. The two groups were comparable in age, number of previous infarctions and severity of attacks.

24% of control patients but only 15% of treated patients died. The use of anticoagulants reduced the death rate by reducing the thrombo-embolic complications occurring throughout the first four weeks following infarction, but most frequently seen during the second week. The death rate, although highest in the first two weeks, was sufficiently high in the first four weeks to justify the use of anticoagulant therapy as late as the second or third week after infarction. Only 6% of the treated group had thrombo-embolic complications as compared with 25% in the control group. In the treated group thrombo-embolic complications were reduced in all age periods, especially the period 50-59 years, whereas in the control group the largest number of thrombo-embolic complications were recorded in this age period. The incidence of severe hemorrhage in the treated group was extremely low: of 30 hemorrhages, 15 were mild, 14 moderately severe and one severe. From the results obtained, the authors concluded that anticoagulant therapy should be used in all cases of coronary thrombosis with myocardial infarction unless a definite contra-indication exists.

H. R. Rowsell

NEUROLOGY

Cerebral Symptoms in Thrombo-Angiitis Obliterans. D. Perk: J. Ment. Sci. **93**, 748-755 (Oct. 1947).

Thrombo-angiitis obliterans of the cerebral vessels may produce tics, epileptiform convulsions, pareses, paralyses, hemianopia, paresthesias, aphasia, apraxia, impoverishment of memory or loss of consciousness. Besides these neurological symptoms, mental symptoms may occur and range from transient confusion or excitement to full-fledged psychoses. An illustrative case is presented.

A. C. Parkin

PHYSIOLOGY

The Physiological Basis of Neuromuscular Disorders. Sir H. Dale: Br. Med. J. *4585* (Nov. 20, 1948).

It is now generally accepted that the effects of impulses in efferent post-ganglionic fibres of the autonomic nervous system are transmitted to involuntary muscles and gland cells by the liberation of two transmitters—epinephrine (sympathin) and acetylcholine. Attention is briefly drawn to the possibility that histamine may be a third transmitter, involved in the so-called "antidromic" nerve impulses. These phenomena of chemical transmission from peripheral involuntary nerve-endings, although well-established experimental facts for over 25 years, have influenced the understanding of clinical conditions but little, their main effect being to clarify the actions of well-known drugs such as atropine, physostigmine, and epinephrine, and to stimulate discovery of new ones, such as carbachol, prostigmine, and flurophosphonates.

Argument is advanced to support the chemical transmission theory at the motor myoneural and ganglionic synapses as a process essentially different from the conduction of the excitatory process along either a nerve or muscle fiber. In neuromuscular disorders, clinical concern centres about the transmitter acetylcholine and its nicotine action on the motor end-plates and autonomic ganglion cells. These structures are sensitive to acetycholine and are made insen-

sitive to it by excess nicotine, by curare or persistent excess of acetylcholine itself. Curare blocks this effect at the motor end-plate by making it specifically insensitive to acetylcholine while leaving it normally responsive to direct electrical stimulation and to the administration of potassium chloride. This is the only sense in which the term "curare-like" action should be used and it should especially not be confused with the action of other poisons such as botulinus or tetanus toxins.

Physostigmine, and recently di-isopropyl-fluorophosphonate (D.F.P.) and tetramethyl-pyrophosphate all exhibit anticholinesterase effects and have proven valuable in myasthenia gravis. No abnormal amounts of cholinesterase have as yet been demonstrated in myasthenia gravis, nor have any curare-like poisons been isolated from the thymus, removal of which, in some cases, produces dramatic results while, in others, it is completely ineffective.

The author discusses briefly the use of the quaternary tetraethyl ammonium salts in hypertension and points out that the tetramethyl salts have a far greater nicotine action than their tertaethyl homologues. If we attribute the hypertension to excess outflow of preganglionic sympathetic impulses we may expect the tetramethyl salts to weaken this transmission.

Finally, the question of chemical transmission in the central nervous system is mentioned and the article is concluded with a reminder that scientific caution is needed in this field to prevent scientific imagination from surpassing present evidence.

B. Cowitz

PSYCHIATRY

The Results of Treatment of a Thousand Cases of Schizophrenia. L. A. Finiefs: J. Ment. Sci. **94**, 575-580 (July 1948).

Of 1009 cases of schizophrenia hospitalized over a period of 17 years, 446 received no special treatment and of these 34.5% were discharged as improved or much improved. Of 82 patients treated with convulsion therapy (in most cases electro-shock), 39% were discharged. Of 103 cases treated with combined electro-shock and insulin-coma therapy, 54.3% were discharged. Of 378 cases treated with insulin-coma therapy alone, 54.2% were discharged. Of the 156 patients discharged after receiving no special treatment, 14.1% remained well for 5 years or longer after an average of 8.3 months' hospitalization. Of 188 patients followed who received special therapies, 62.2% remained well for 5 years or longer after an average of 5 months' hospitalization. The author concludes that the insulin treated group not only made a greater percentage of recoveries but also spent less time in hospital both initially and subsequently.

A. C. Parkin

SURGERY

Carcinoma of the Stomach. Park and McNeier: Surgery **24**, 769-778 (Nov. 1948)

This is an analysis of 795 cases of carcinoma of the stomach—one of the most common and most rapidly fatal of carcinomata. In the years 1916-1930, 2.9% of 272 patients had resectable lesions. In contrast, from 1942 to 1946, the resectable rate was 39.8%. Of the patients subjected to laparotomy, 82% had a resection either curative or palliative and 34.7% of these had a five-year cure. The rate can be correlated with the introduction of total gastrectomy and transthoracic resection of the cardia, with a reduction in the mortality rate from 62.5% to 7.8%. The conclusions drawn from the analysis were: (*a*) the preoperative duration of symptoms has no influence on curability; (*b*) carcinoma *in situ*—ulcer and polypoid types—have the highest five-year cure rate averaging 80%, whereas the more common infiltrating and colloid carcinomata have the lowest rate, 20%; (*c*) patients with metastases showed a five-year rate of 24.2% in contrast to the rate of 42.8% in those without metastases and (*d*) local fixation influences the survival rate favourably because it leads to more radical surgery. Surgeons are urged to attempt as radical a resection as possible because only this procedure will result in a high rate of cure.

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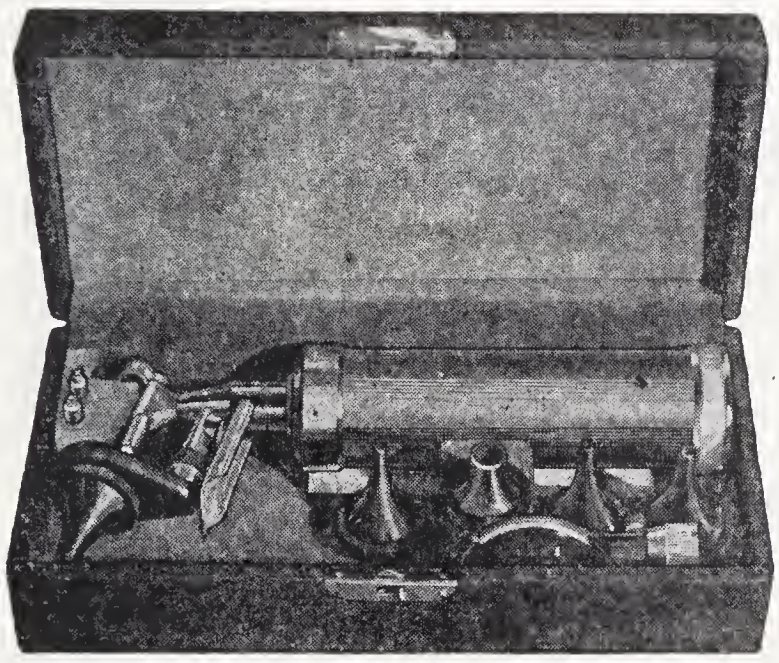

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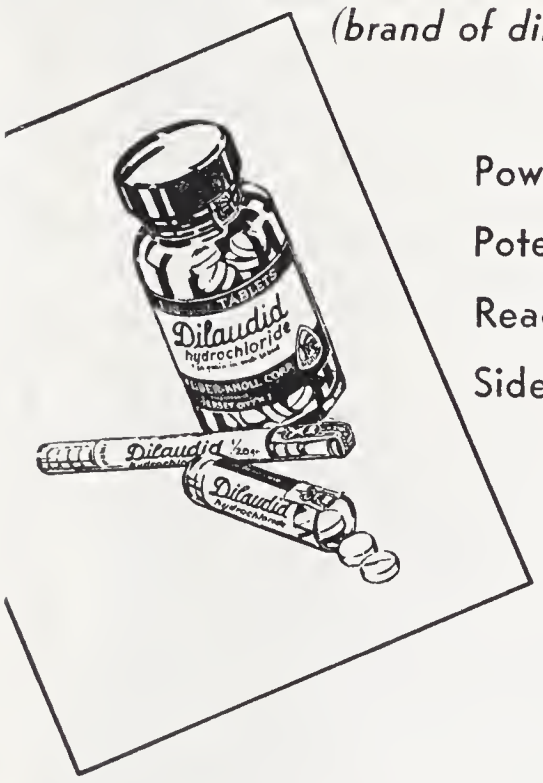

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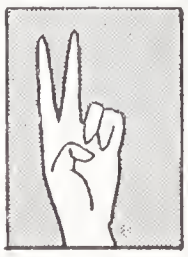

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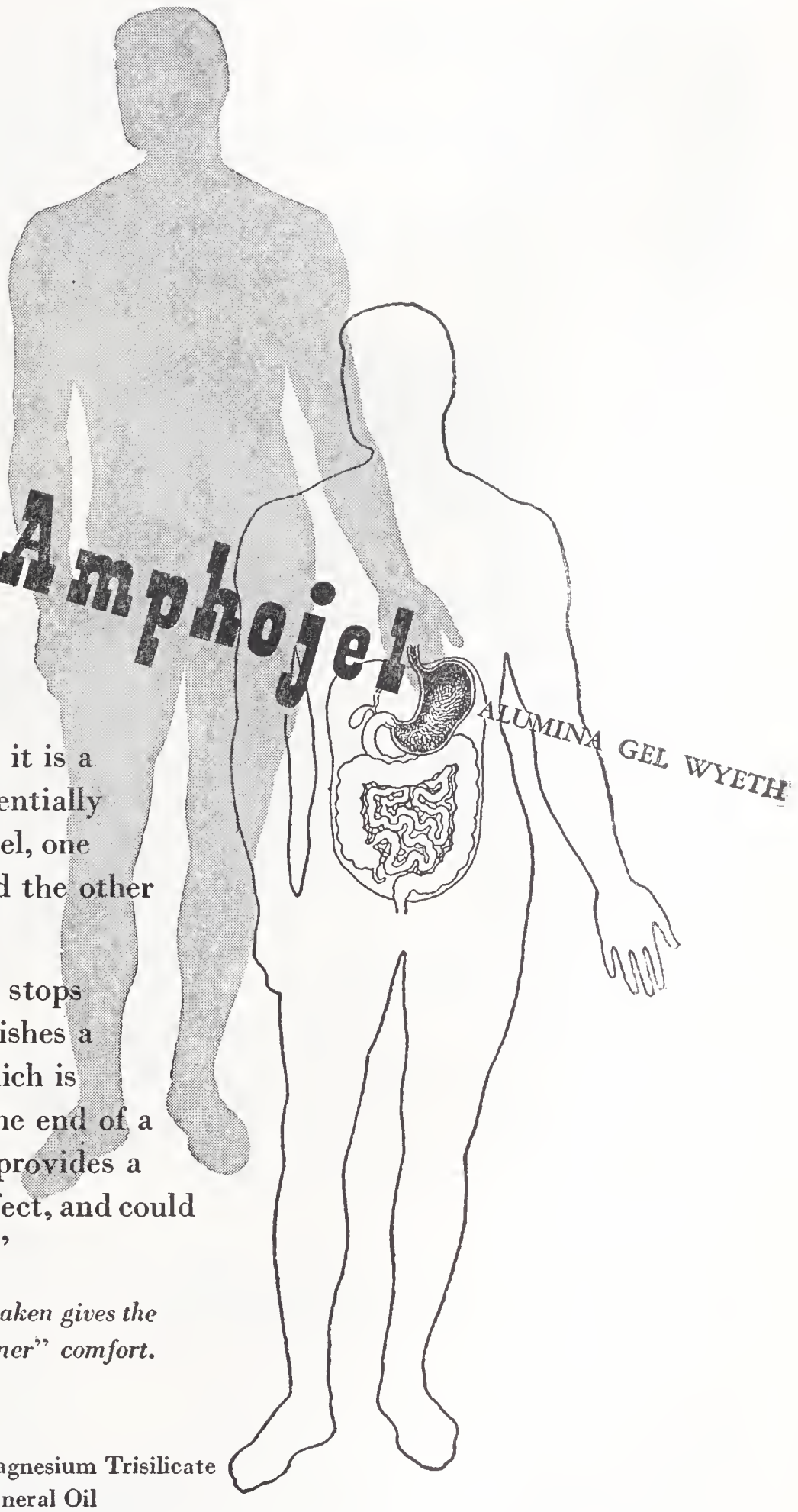

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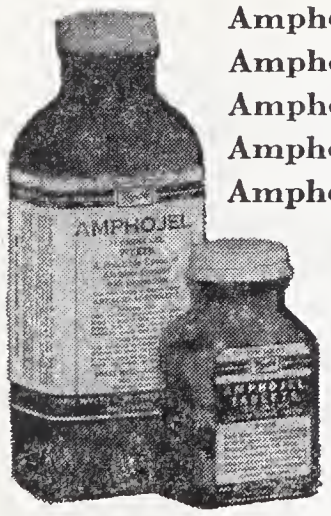

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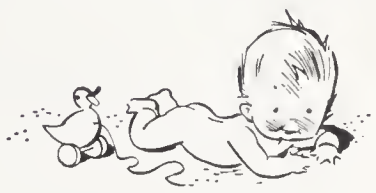

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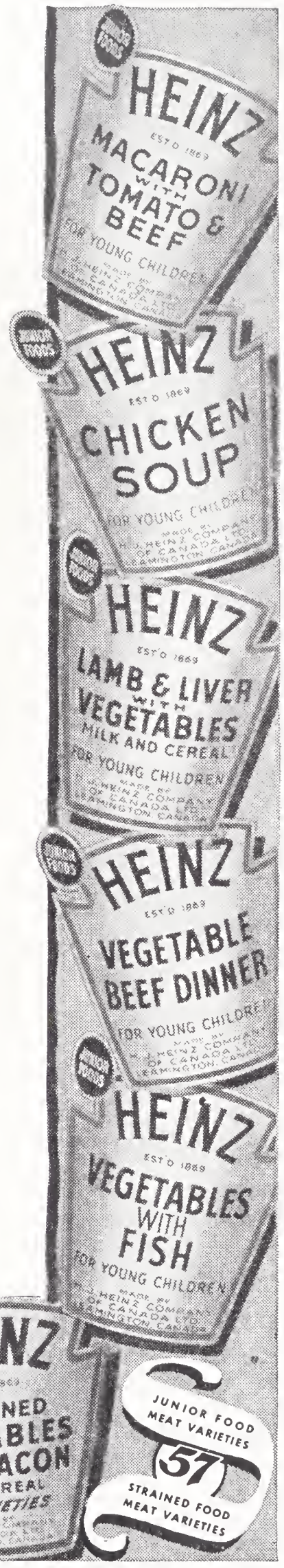

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